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The role of sleep and dreaming in the processing of episodic memory

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The role of sleep and dreaming in the processing of episodic memory

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RÉSUMÉ

La présente thèse examine les liens entre le sommeil, la mémoire épisodique et les rêves. Dans une première étude, nous utilisons les technologies de la réalité virtuelle (RV) en liaison avec un paradigme de privation de sommeil paradoxal et de collecte de rêve en vue d'examiner l'hypothèse que le sommeil paradoxal et le rêve sont impliqués dans la consolidation de la mémoire épisodique. Le sommeil paradoxal a été associé au rappel des aspects spatiaux des éléments émotionnels de la tâche RV. De la même façon, l'incorporation de la tâche RV dans les rêves a été associée au rappel des aspects spatiaux de la tâche. De plus, le rappel des aspects factuels et perceptuels de la mémoire épisodique, formé lors de la tâche VR, a été associé au sommeil aux ondes lentes. Une deuxième étude examine l'hypothèse selon laquelle une fonction possible du rêve pourrait être de créer de nouvelles associations entre les éléments de divers souvenirs épisodiques. Un participant a été réveillé 43 fois lors de l'endormissement pour fournir des rapports détaillés de rêves. Les résultats suggèrent qu'un seul rêve peut comporter, dans un même contexte spatiotemporel, divers éléments appartenant aux multiples souvenirs épisodiques. Une troisième étude aborde la question de la cognition lors du sommeil paradoxal, notamment comment les aspects bizarres des rêves, qui sont formés grâce aux nouvelles combinaisons d'éléments de la mémoire épisodique, sont perçus par le rêveur. Les résultats démontrent une dissociation dans les capacités cognitives en sommeil paradoxal caractérisée par un déficit sélectif dans l'appréciation des éléments bizarres des rêves. Les résultats des quatre études suggèrent que le sommeil aux ondes lentes et le sommeil paradoxal sont différemment impliqués dans le traitement de la mémoire épisodique. Le sommeil aux ondes lentes pourrait être implique dans la consolidation de la mémoire épisodique, et le

sommeil paradoxal, par l'entremise du rêve, pourrais avoir le rôle d'introduire de la flexibilité dans ce système mnémonique.

Mots clefs: mémoire épisodique; sommeil paradoxal; sommeil aux ondes lentes; rêves; réalité virtuel

SUMMARY

The present dissertation examines relationships between sleep, episodic memory and dreaming. In Articles I and II we use a novel virtual reality (VR) task in conjunction with a rapid eye movement (REM) sleep deprivation (REMD) paradigm and dream sampling to examine the hypothesis that REM sleep and dreaming are involved in the consolidation of episodic memory. REM sleep was associated with the successful retrieval of the spatial aspects of emotionally charged elements of the VR task. Similarly, dreaming was associated with improved performance on the spatial aspects of the retrieval task. Retrieval of the factual and perceptual aspects of episodic memories formed with the VR task was associated with increased slow wave sleep (SWS) during the post-exposure night. Overall, the results suggest that SWS is associated with the perceptual and factual aspects of episodic memories while REM sleep is not, a finding which may relate to observations that REM sleep dreaming is composed of deconstructed fragments of loosely associated episodic memories. Study II examines the hypothesis that a function of dreaming may be to create new associations between previously unrelated memory items. A participant, highly trained in introspection and mentation reporting, was awakened 43 times during theta bursts at sleep onset and provided detailed reports of resulting imagery and associated memory sources. This technique provided evidence that elements of distally related memory sources are brought together in temporal and spatial proximity within a novel context provided by the dream, suggesting a role for dreaming in memory processing. To allow for this possibility, we speculate that dreaming experiences may be functionally equivalent to waking experiences in their ability to induce neural plasticity. Study III

addresses an aspect of this functional equivalence by examining if dream bizarreness is incompatible with behavioral and cognitive features associated with waking state experience-driven plasticity, i.e., whether the dreamer can act upon, emote and be motivated towards an element of the dream that is bizarre and that violates basic assumptions of physical reality. The results demonstrate a dissociation in cognitive ability during dreaming characterized by a selective deficiency in appreciating bizarreness in face of a maintained ability for logical thought. This finding thus addresses the problem of the wake-like mind reflecting upon dream bizarreness and suggests that dreaming is a state in which the cognitive aspects associated with synaptic plasticity (attention, emotion and motivation associated with believing a situation to be reality) are present while allowing for the presentation of memory item combinations which may transcend the limits of physical reality. The results of the four studies are discussed in light of how REM and SWS sleep stages are differentially involved in specific aspects of episodic memory (episodic replay vs. episodic novelty) and the possible role that dreaming, as a driver of synaptic plasticity, may have in these relationships.

Key words: episodic memory, REM sleep, slow wave sleep, dreaming, virtual reality.

TABLE OF CONTENTS

LIST OF TABLES

LIST OF FIGURES

LIST OF ABBREVIATIONS

DLPFC: Dorsal lateral prefrontal cortex

fMRI: Functional magnetic resonance imaging

HC: Hippocampus

LTP: Long-term potentiation

LTD: Long-term depression

NC: Neocortex

NREM: Non-rapid eye movement

NREM1: Non-rapid eye movement stage 1 sleep

NREM1Φ : Non-rapid eye movement stage 1 sleep, theta burst sub stage.

OCD: Obsessive compulsive disorder

PET: Positron emission tomography

PGO: Ponto-geniculo-occipital

PTSD: Post traumatic stress disorder

REM: Rapid eye movement

REMD: REM sleep deprivation

REMs: Rapid eye movements

SO: Sleep onset

SWR: Sharp wave ripple

SWS: Slow wave sleep

VR: Virtual reality

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CHAPTER I

General introduction

Preface

It is unclear why we sleep. In recent years a veritable explosion of research has led researchers to propose several functions for sleep, including the restoration of cellular components (Mignot, 2008) and the conservation of energy (Zeplin et al., 2005). However, these functions do not explain why sleeping is associated with the loss of awareness of the environment, a change that renders animals particularly vulnerable to predators, and yet has been selected for evolutionarily in almost all vertebrates. One intriguing possibility is that during sleep memory systems undergo processing that interferes with conscious awareness of the environment. For example, it has been proposed that immediate processing of information and its long-term storage utilize the same limited neural networks (Marshall and Born, 2007). Because of the restricted capacity of these neural networks, the brain can either process new information *or* consolidate information for long-term storage, but not both at the same time. While this hypothesis is applicable to slow wave sleep (SWS) that is typically void of conscious experiences, it stands in conflict to mounting phenomenological and neurophysiological evidence that consciousness and vivid sensory experiences are present during REM sleep dreaming. Could the sensory experiences occurring during dreaming therefore play a role in memory processing in REM sleep?

The present thesis examines this question. Memory is a subjective experience, and this is particularly true for episodic memories where life events are replayed in some of their initial perceptual richness. It is these life moments that interact with dreams wherein fragments of episodic memories appear to be woven into novel experiences. Indeed, both episodic memory and dreaming concern the visualization of events that occur within a distinct spatial-temporal context, but that use memory sources in opposing ways. Episodic memory deals with recreating past events, while dreaming deals with creating novel events with memory items that may be loosely associated.

One reason why the link between memory consolidation and dreaming has not been properly examined is that episodic memory and dreaming concern realistic life events, yet

the experimental stimuli used in memory tasks typically consist of word lists and decontextualized pictures. To overcome this methodological limitation, we programmed a virtual reality (VR) task that allows subjects to participate in lifelike events in a systematic manner and in a carefully controlled environment. We expected that immersing participants in a lifelike VR environment would lead to the creation of contextually and visually rich episodic memories even while key aspects of the environment could be experimentally controlled. We used the VR task in conjunction with a REM deprivation (REMD) procedure to examine the role of REM sleep and dreaming in episodic memory processing during sleep. Contrary to expectations, results indicated that REM sleep and dreaming were associated only with learning the spatial locations of items in the episodic memory task whereas SWS is associated with the consolidation of factual and perceptual features of episodic memory. We also observed that the VR task was incorporated into dreaming in a fractionated manner.

We subsequently examined whether dreaming is involved in creating novel, meaningful associations between memory items. A participant trained in introspection was repeatedly awakened during theta bursts at sleep onset. The procedure resulted in numerous and highly detailed reports of dreaming and associated memory sources. Results suggest that dreaming incorporates items from distal memories in a manner that may promote integration among memories spanning one's lifetime.

Finally, we examined the perception of bizarreness in dreaming. The results indicate that during dreaming subjects report a diminished awareness of bizarreness in face of a maintained ability to engage in logical thinking. This particular sleep-dependent cognition allows for bizarre memory item combinations within the dream to be perceived as "normal", thus allowing the dreamer to interact, emote and be motivated towards bizarre elements of the dream in the same manner as elements that are compatible with waking reality.

The results of these studies together support the notion that SWS and REM sleep are implicated in different aspects of episodic memory consolidation. SWS may be implicated in consolidating memories resulting from experience-induced plasticity (i.e.,

learning). In contrast, REM sleep may be involved in a complementary process that generates flexibility within memory representations via experience-induced plasticity resulting from dreaming.

Introduction

During sleep the brain cycles though a series of successive states characterized by unique patterns of cerebral, physiological and psychological activity. The widely adopted Rechtschaffen and Kales (1968) method for sleep scoring divides human sleep into five stages based predominantly on the frequency of brain oscillations: stage 1 as a shift from of alpha activity (8-13Hz) to theta activity (5-7 Hz), stage 2 as containing bursts of sigma activity (sleep spindles) and brief negative high-voltage peaks (K-complexes), stage 3 and stage 4 as the presence of delta activity (0.2-2 Hz) and REM sleep as desynchronized activity with a predominance of theta that is accompanied by rapid eye movements and a large reduction in muscle tone (atonia). Because of the behavioural particularities of REM sleep, including its close association with dreaming, sleep stages 1, 2, 3 and 4 were distinguished from this state and collectively referred to as non-REM (NREM) sleep (Dement et al., 1957).

A large body of research has sought to clarify the neurobiology and psychophysiology of sleep, and has done so largely within the Rechtschaffen and Kales (1968) scoring framework. More recently, advances in brain imaging and intra-cranial recording techniques have provided unprecedented observations of the brain while asleep. These results are summarized briefly in the following sections and Table 1.

Sleep Neurophysiology & Psychophysiology

REM sleep

REM sleep is found only in mammals and birds and has been studied primarily, but not exclusively, in humans, cats and rats (see Tobler, 1995 and Siegel, 2008 for reviews). Compared to all other sleep stages, REM sleep is characterized by increased levels of brain activity and increased levels of whole body metabolism. The early discovery that REM

sleep consisted of a highly active brain in face of reduced behavioral activity led early investigators (Jouvet & Michel, 1959) to refer to this state as paradoxical sleep, a term widely used today in animal research. REM sleep is characterized by an organized set of phenomena that differentiates it from other stages of sleep. For the identification of REM sleep, the standard scoring method (Rechtschaffen & Kales, 1968) requires three physiological events to co-occur within a 20-30 second epoch: 1) rapid eye movements (REMs), 2) reduction of muscle tone (atonia) and 3) fast, desynchronized, low voltage EEG featuring theta band activity. REM sleep can be further categorized into phasic and tonic on the basis of the presence or absence of REMs, respectively.

Positron emission tomography (PET) studies characterize REM sleep as a state of selective prefrontal deactivation and increased limbic activation. These and other regional changes are taken to indicate selective processing of emotional memories (Maquet et al., 1996), processing of information in isolation of external inputs and motor outputs (Braun et al., 1997) and integration of the executive capacities of the neocortex with motivational and reward capacities of the basal forebrain and hypothalamus (Nofzinger et al., 1997). A more recent meta-analysis of several PET studies of REM sleep (Maquet et al., 2005) has revealed hypoactivation of specific areas within the parietal lobes and the dorsolateral prefrontal cortex (DLPFC) and other prefrontal regions.

Overall, these observations are consistent with reports that REM sleep dreaming is emotional in nature and characterized by diminished capacity to reason (Hobson et al., 2000). Indeed, since the first investigations of REM sleep (Aserinsky and Kleitman, 1953; Dement and Kleitman, 1957), dreaming has been closely associated with this stage of sleep. While dreaming is reported from other stages of sleep (Nielsen, 2000), REM sleep is associated with dreaming that is longer, more frequent, more perceptually vivid, more emotional, and less related to waking life (see review in Hobson et al., 2000).

During REM sleep the hippocampus is active and hippocampal reactivation of pre-sleep exploratory behavior is observed at the cellular level in rats (Louie & Wilson, 2001). The hippocampus and the amygdala are co-activated and synchronized in the theta frequency band at this time (Pare & Gaudreau, 1996; Hegde, et al., 2008; Karashima et al,

2010). Ponto-geniculo-occipital (PGO) waves (or P-waves in animals) are recorded from the pons, the lateral geniculate nucleus, and the occipital regions of the brain during REM sleep and are associated with REMs (Datta and Hobson 1994; Datta 1995). Hippocampal/amygdalar theta synchronization is enhanced in association with increased PGO wave density (Karashima et al., 2010).

Stage 3 & 4 sleep (SWS sleep)

Stages 3 and 4 sleep are characterized by high-voltage 1-4 Hz slow oscillations originating in the neocortex (Achermann & Borbely, 1997). Stage 3 contains 25-50% of slow wave activity and stage 4 contains over 50%. For this reason, these two stages are often grouped together and referred to as slow wave sleep (SWS). SWS is only found in mammals and birds (Siegel, 2005) and has been studied predominantly in the rat where, like in REM sleep, cellular activity in the hippocampus associated with pre-sleep exploratory behavior during wake was observed (Wilson & McNaughton, 1994; Lee & Wilson, 2002; Ji & Wilson, 2007). This hippocampal reactivation occurs in conjunction with sharp wave ripples (Wilson & McNaughton, 1994; Molle et al., 2006; Peyracheet al., 2009), high-frequency oscillations originating from the hippocampus that are also found in waking state. In contrast to REM sleep, hippocampal reactivation in SWS is paralleled by cellular replay in neocortical areas such as the prefrontal (Peyrache et al., 2009), parietal (Qin et al., 1997) and visual cortex (Ji & Wilson, 2007). Early PET studies (Maquet et al., 1997; Braun et al., 1997) characterized SWS in terms of an overall reduction of activity in cortical and thalamic areas. A later fMRI study (Kaufmann et al., 2005) identified only localized areas of reduced activity, as compared to wakefulness, in frontal areas, association cortices, cingulate cortex, hippocampus, thalamus and hypothalamus. Moreover, small clusters of increased activation were found in the inferior frontal gyrus, temporal areas, the cerebellum and the parahippocampal areas. Similarly, a recent study (Dang-Vu et al., 2008) found slow oscillations to be correlated with increases in activity across several cortical areas, effectively challenging the notion that SWS is characterized by overall brain quiescence.

Dreaming is found after awakenings from SWS although less frequently than awakenings from REM sleep (for review see Nielsen, 2000). In one study, one to five additional nights were required in order for 20 of 60 participants to report any form of mentation from SWS, while 10 of 60 participants reported no mentation at all from this stage (Cavallero et al., 1992).

Stage 2 sleep

Stage 2 sleep is characterized by the presence of sleep spindles, which consist of 11–16 Hz phasic oscillations with a fusiform shape and of approximately 500 ms (Gibbs et al., 1950), and K-complexes, which are brief, negative, high-voltage peaks followed by a slower positive complex and a final negative peak (Roth et al., 1956). Stage 2 is characterized by decreased activity in adjacent regions of the temporal lobe, the inferior parietal lobule and the inferior/middle frontal gyri, the cingulate cortex, the right insula and thalamic and hypothalamic regions (Kaufmann et al., 2006). The functional meaning of these patterns of activation is still unclear.

Stage 1 sleep

The transition from wake to sleep occurs during NREM sleep stage 1 (NREM1). NREM1 sleep is characterized by a series of alternating periods marked by alpha trains, theta ripples, or vertex waves. Hori et al. (1994) proposed that these patterns can be classified into 9 sub-stages starting with alpha wave trains (sub-stage 1; wake state), intermittent alpha >50% (sub-stage 2; wake state); intermittent alpha <50% (sub-stage 3; NREM1), EEG flattening (sub-stage 4; NREM1 sleep), theta waves (sub-stage 5; NREM1 sleep), solitary humps or solitary vertex waves (sub-stage 6; NREM1 sleep), hump trains or vertex waves (sub-stage 7; NREM1 sleep), humps or vertex waves with incomplete spindles (sub-stage 8; NREM1 sleep) and stage two sleep with spindles (sub-stage 9; stage 2 sleep).

Very few studies have examined the neurobiology of NREM1 sleep, and no brain imaging or intra-cranial studies have assessed the Hori sub-stages. fMRI studies do depict

stage 1 as a state of reduced thalamic and cingulate activity, increased occipital (precuneus) and temporal activity (Kaufmann et al., 2006.) and increased hippocampal activity (Picchioni et al., 2008). A MEG study found that gamma-band activity increases in precuneus during stage 1. A recent fMRI study comparing the first 30 seconds vs. the last 30 seconds of NREM1 sleep found an increase of hippocampal activity during the last 30 seconds (Picchioni et al., 2008). Hippocampal activity that is normally characteristic of REM sleep has been found also to characterize NREM1 sleep (Bódizs et al., 2005; 2008). In a recent fMRI study, Magnin and colleagues (2010) found thalamic deactivation occurring several minutes before cortical deactivation at sleep onset, but synchronized reactivation of both structures during awakening.

Several similarities between REM and NREM1 sleep, including hippocampal activation, increased theta band activity, vivid dream mentation, and the sensitivity of both states to REM sleep deprivation, support the proposal that NREM1 sleep is a brief episode of REM sleep (see Nielsen, 2000 for review) that can be more easily assessed experimentally for evidence of REM sleep-related memory processing. Indeed, if participants are probed for the presence of mentation, dream-like visual experiences are reported after NREM1 sleep awakenings with a prevalence as high as after REM sleep awakenings (Germain and Nielsen, 1997; Hayashi et al., 1999; Nielsen et al., 2005).

Sleep stages and "covert" sleep phenomenon

Some sleep features such as spindles and slow oscillations are not unique to a single stage but found across several; other features such as theta and slow wave ripples are also found in wake. Reports that REM sleep atonia (Werth et al., 2002) and rapid eye movements can be found in Stage 2 sleep suggest that sleep stages are fluid as opposed to all-or-nothing segregations (Nielsen, 2000). The traditional scoring system requires the presence of a specific quantity of slow oscillations for SWS and the co-occurrence of multiple, physiological events for REM sleep (i.e., REMs, atonia and wake-like EEG). Yet phenomena related to REM sleep and SWS are found beyond borders established by the standard scoring criteria of Rechtschaffen and Kales (1968). The Covert REM (C-REM)

model (Nielsen, 2000) posits that dreaming outside of REM sleep (e.g., NREM1) is nonetheless associated with REM sleep-phenomena such as eye movements, hippocampal activity or muscle atonia that can be expressed in non-REM sleep stages of sleep in a partial, dissociated or covert manner. This model accounts for why dreaming is primarily associated with REM sleep but can also be found in other stages of sleep, albeit less frequently. As can be seen in Table 1, stages of sleep in which elements of REM sleep are found are also those featuring the most frequent and vivid dreaming.

Table 1. Phenomena associated with sleep and their typical distribution across sleep stages and wake.

X = Defining feature
x = Feature sometimes present

	Wake	NREM1	Stage 2	SWS	Phasic REM	Tonic REM
Distribution across a sleep period			Late & early sleep	Mostly early sleep	Mostly late sleep	Mostly late sleep
Slow oscillations			X (K-Complex)	X		
Theta	x	x			X	X
Spindles			X	x		
PGO	X				X	
Slow wave ripples	X			X		
Atonia		x	x		X	X
Wake-like eye movements	X	x			X	
Mentation		Frequent	Less frequent	Rare	Frequent	Frequent

The functions of sleep and sleep stages

Numerous functions of sleep have been proposed. Of these, three have received substantial empirical scrutiny (Mignot, 2008). First, it is proposed that sleep reduces energy demands (Zepelin et al., 2005). However, this hypothetical function does not appear to apply to REM sleep as the latter is characterized by an augmented energy expenditure, e.g., increased whole body oxygen consumption (Parmeggiani, 2003). This function also does not explain why consciousness is lost during sleep, a factor which

heightens vulnerability to predators. A second proposed function is that sleep plays a role in restoring cellular infrastructure, such as the replenishment of macromolecules (Huber et al., 2006) and transmitter vesicles (Mignot, 2008). However, this possible function, too, concerns mostly NREM sleep stages (Mignot, 2008). A third proposed function is a role for sleep in memory processing. A growing body of evidence supports the notion that sleep is not only involved in, but also sometimes critical for, the consolidation of learning and memory. And, in contrast to the previous two proposed functions, this function includes roles for both REM and NREM sleep. Only the latter function will be considered in more detail here.

Before reviewing results from studies that have examined sleep stages in relationship to memory, a brief overview of memory systems is presented.

Memory Systems

Memory consolidation refers to the time-dependent processes of strengthening or stabilizing labile memory traces, converting them into more long-lasting forms. Memory systems are divided into two broad categories that differ, in large part, in whether learning and retrieval are accompanied by conscious awareness (i.e., declarative memory) or not (non-declarative or procedural memory) (Cohen & Squire 1980). These two memory systems may also differ in that individuals have voluntary access to declarative memories whereas non-declarative learning is stimulus driven (Squire, 1992). For instance, tasks such as texture discrimination or motor learning, where participants are not explicitly aware of encoding and retrieval when learning, are considered to require non-declarative memory. The non-declarative memory system includes conditioning, priming, and procedural memory (e.g., motor and visual discrimination skills). In contrast, the declarative memory system is consciously accessible.

Declarative memory is composed of both semantic and episodic types of memory (Tulving 1983). Semantic memory consists of general knowledge (e.g., London is the capital of England) whereas episodic memory describes memory for specific events (Boarding the London subway for the first time). The retrieval of an episodic memory is

the ability to recreate, in some perceptual detail, a moment that had previously been experienced. In this sense, episodic memory enables one to "travel back in time" to reexperienced events (Tulving, 2002). Thus, central to episodic memory is the re-experiencing of unique events, specified in time ('when') and space ('where'). Each episodic memory thus has a unique context consisting of the temporal, spatial and perceptual details surrounding an event. Also central to episodic memory is the concept of autonoetic awareness, i.e., a conscious recollection of the original events by mentally reliving them. In contrast, noetic awareness refers to the knowledge that an event has occurred without the ability to consciously recollect the event itself.

Autobiographical memory refers to episodic memories of personally relevant events. It is a term often appearing in models arguing the interconnectedness of the self with memory (e.g., the self-memory system; Conway & Pleydell-Pearce, 2000). The term is also used by some authors to refer to episodic memories that span an individual's entire life (e.g., Steinvorth et al., 2005). Autobiographical memories are a subset of episodic memories and will therefore not be expanded upon further.

It is generally agreed that the declarative memory system is critically dependent on the hippocampus and medial temporal lobe more generally (Cohen & Squire 1980; Squire 1992; Squire et al. 2004) whereas non-declarative memory is independent of the hippocampus (Spiers et al. 2001; Squire et al. 2004). According to the standard consolidation theory (Squire, 1986; 2004), an episodic memory is dependent upon the hippocampus for a time-limited period. It undergoes a consolidation process involving the transfer of information from hippocampal areas to distributed neocortical sites and thereby eventually becomes independent of the hippocampus. In contrast, the multiple trace theory (Nadel & Moscovitch, 1997) posits that the hippocampus is always required for the acquisition and recollection of episodic memories. It is responsible for providing the spatial-temporal context with which neocortical traces are bound into a coherent representation during recall ('binding'). Episodic memory recall is thus a constructive process that involves the re-activation of a hippocampal-neocortical trace. Nonetheless,

with repetition and rehearsal multiple traces are created and therefore episodic memories become more resistant to hippocampal damage.

Sleep and memory

Studies examining REM sleep and memory

REM sleep deprivation studies

Several techniques used to examine the role of REM sleep in learning and memory in humans are summarized in Table 2. One method consists of reducing REM sleep prior to a task and assessing if subsequent learning is disrupted. Using this technique, REM sleep deprivation resulted in reduced performance on the Guilford Utility Test (Lewin & Glaubman, 1975), which measures divergent thinking.

A second method involves reducing the amount of REM sleep after having participants learn a task and examining the consequences for subsequent performance, a technique widely referred to as post-learning REM sleep deprivation. This form of REM sleep deprivation was found to have a detrimental effect on the recall of meaningless sentences and anomalous prose passages (Empson & Clarke, 1970), anagram solutions (Grieser et al., 1972), the recall of adjectives indicative of personal dissatisfaction (Cartwright et al., 1975), a visual discrimination task (Karni et al., 1994), the Wff'n Proof complex logic task, (Smith 1993; Smith & Lapp, 1986), word fragment completion, the Corsi block tapping task and the Tower of Hanoi (Smith, 1995). REM sleep deprivation was also found to have a detrimental effect on the retention of stories (Empson et al., 1980; Tilley and Empson, 1978). It is of note that Tilley and Empson (1978) found that small amounts of REM sleep deprivation could significantly decrease the accuracy of recalling a story. Although the emotional character of the stories used in these studies was not explicitly mentioned, one story utilized by Tilley and Empson (1978) "The war of the ghosts", was considerably emotional in nature. Similarly, Wagner et al., (2001) found that curtailing late night sleep, which is rich in REM sleep, was associated with poor retention of emotional, but not neutral, stories. This study used an alternative method of REM sleep

deprivation that takes advantage of the fact that the proportion of SWS decreases through the sleep period while the proportion of REM sleep increases.

Using the same REM sleep deprivation method, it was found that reduction of late night sleep was associated with worsened performance on the mirror tracing task, but not on the recall of word pairs (Plihal and Born, 1997). Late night sleep was also associated with an episodic-like task measuring the 'what' 'where and 'when' features of word list information (Rauchs et al., 2004). Specifically, curtailment of late sleep was associated with worsened recall of 'where' and 'when' information, as well as with lower recall of contextual details of encoding, a measure of autonoetic awareness.

Some studies have utilized pharmacological interventions to suppress or alter REM sleep. In one study, a nicotinic receptor antagonist mecamylamine, that induces cholinergic receptor blockade, impaired the consolidation of a finger sequence tapping task but did not affect word-pair memory (Rasch et al. 2009). This result suggests that high levels of acetylcholine in REM sleep may be critical to the consolidation of motor memories. In a second study, Rasch et al. (2009) found that selective serotonin or norepinephrine re-uptake inhibitors, that suppress REM sleep, did not disrupt memory consolidation for word pairs and, surprisingly, enhanced memory for finger-tapping skills.

REM sleep deprivation does not negatively impact all types of memory task however (see Table 2). It was found not to disrupt the learning of trigrams (Chernik, 1972) or performance on a word fluency test (Lewin & Glaubman, 1975). It was also found to have no detrimental effect on memory tasks such as verbal paired associates (Castaldo et al., 1974; Chernik, 1972; Ekstrand, 1972; Ekstrand et al., 1971; Genzel et al., 2009; Lewin & Glaubmann, 1975; Smith, 1993) serial or clustering verbal memory (Lewin & Glaubman, 1975), serial word lists (Empson & Clarke, 1970), word recognition or visual non-verbal figures (Smith, 1995), mirror-tracing (Tweed et al., 1999) or sequential finger-tapping (Genzel et al., 2009).

Post-training REM sleep modulation studies

Another class of studies has determined whether learning is associated with subsequent changes in REM sleep parameters. Typical REM sleep parameters include REM sleep % (proportion of total sleep time occupied by REM sleep), REM sleep time (total time in REM sleep) and REM density (frequency of REMs per unit of time).

Changes in REM sleep parameters were found following administration of the Wechsler Adult Intelligence Scale (increased REM time, REM sleep % and number of REM periods) (Feinberg et al., 1973), viewing of an anxiety arousing film (increased REM sleep respiratory irregularity; Baekland et al., 1968) (increased REM density; Goodenough et al., 1975), exposure to a task eliciting curiosity, emotions and divergent thinking (increased REM time) (Lewin & Gombosh, 1973), exposure to ego-threatening social interactions (increased REM density) (Cohen, 1975), successful completion of Thematic Appreciation Test solutions (increased REM %) (Cartwright, 1974), intensive learning during summer exams (Smith & Lapp, 1991) and the novel complex motor learning required for trampolining (increase in REM sleep %) (Buchegger et al., 1988; 1991). Some studies report correlations between learning and REM sleep variables, such as positive correlation between retention of Morse code learning and REM sleep duration, number of REMs and REM density (Mandai et al., 1989). Fischer et al (2002) report an association between REM sleep % and learning of a sequential finger tapping task. Stickgold et al., (2000) found that REM sleep % in the fourth quarter of the night and SWS in the first quarter of the night strongly correlated with learning on the visual discrimination task.

DeKoninck and colleagues examined dreaming as a function of learning and its effects on REM sleep variables. Wearing vision-inverting lenses produced an increase in REM sleep %, while adaptation to them was associated with a reduced REM density (DeKoninck & Prevost, 1991; DeKoninck et al., 1996). Further, those better adapted to the lenses reported dreams that contained more visual and motor difficulties. In a third study by this group, increases in REM sleep % were found to be correlated with learning a second language in a total immersion setting. Students demonstrating higher rates of learning reported communicating the most in French during dreaming and also reported

that French was introduced earlier in the dreaming diaries (DeKoninck et al., 1989). Similarly, Smith and Hanke (2004) found evidence that participants incorporate elements of a mirror tracing task into dreaming, although a relationship between task-related incorporation and performance was not demonstrated.

A study by Smith (2004) took into consideration the intelligence levels of participants in performing the Tower of Hanoi and mirror tracing tasks. Posttraining increases in REM densities and learning were found in participants with the higher intelligence scores. Another study found that REM density was correlated with performance in a pursuit rotor task in low-skill participants only (Peters et al., 2007).

Although not typically considered a REM sleep parameter, theta band activity in REM sleep has also been associated with learning. Fogel et al., (2007) found theta power increases at central regions during REM sleep following paired associates learning. The presence of REM sleep and theta band activity in naps was found to be associated with memory for emotional but not neutral pictures (Nishida et al., 2009).

In another nap study, the presence of REM sleep was associated with creative problem solving measured by the remote associates task (Cai et al., 2009). Similarly, as compared to a period of post training NREM sleep, REM sleep was associated with accurate solving of anagrams, but not trigrams (Scrima, 1982).

A series of PET studies by Maquet and colleagues have demonstrated the effects of an implicit learning task (a serial reaction time task) on posttraining brain activation during REM sleep. Relative to the brains of non-trained subjects, those of subjects trained on the task revealed that many areas activated during waking state learning of the task were also more active during REM sleep (Maquet et al., 2000). A subsequent study showed an increase in functional connectivity between the left posterior parietal cortex and bilateral pre-supplementary motor areas in the trained participants (Laureys et al., 2001). In a third study, REM sleep specific posttraining functional connections between the reactivated cuneus and the striatum were found in relation to the implicit acquisition of the probabilistic rules that defined stimulus sequences, leading the authors to hypothesize that

reprocessing and optimization of available high-order information occurs in REM sleep (Peigneux et al., 2003).

Again, not all memory tasks have resulted in post-training REM sleep changes. No changes were observed for learning verbal paired associates (Castaldo et al., 1974, experiment 1; Bertini & Torre, 1973; Yaroush et al., 1971; Fowler et al., 1973), trigram serial list learning (Castaldo et al., 1974), recall of nonsense-shape paired associates (Fowler et al., 1973), crossword puzzles or the remote-associates task (Cartwright, 1974).

Cueing Studies

Another technique for assessing the implication of REM sleep in learning and memory consists of presenting a task-associated sound during REM sleep as a means of "cueing" a reactivation of the task at this time. After having participants learn Morse code, Guerrien et al., (1989) presented a task-related sound during the eye movements of REM sleep and found greater improvements in performance on a later test than did a group for whom the task-related sound was presented during quiescent lulls between the eye movements. A similar but better controlled experiment involving a complex logic task (Wff'n Proof logic task) found that playing a sound that had been associated with the task during the eye movements of REM sleep led to more improvement on a subsequent performance test than did presentation of the sound during quiescent lulls (Smith and Weeden, 1990). Finally, using rose odor as a cue during REM sleep, Rausch et al. (2007) failed to see any improvement on either finger-tapping or visual-motor tasks.

Discussion of REM sleep and memory studies

A number of trends can be observed from REM sleep /learning studies. First, tasks requiring divergent thinking and cognitive flexibility are consistently associated with REM sleep. Positive findings were reported in cases in which 1) divergent thinking was directly assessed, e.g., with the Guilford's utility test (Lewin & Glaubman, 1975), 2) divergent thinking was a component of the test, e.g., Lewin & Gombosh (1973), and 3) divergent thinking was only indirectly involved, e.g., the Thematic Apperception Test (Cartwright,

1974). Second, tasks involving cognitive flexibility, such as anagram tasks (Greiser et al., 1972; Scrima, 1982) and the remote-associates task (Cai et al., 2009), show a dependence on REM sleep. One exception was a study finding no changes to REM variables following training in the remote-associates task (Cartwright, 1974), although it is not clear what dependent variables were used to determine this lack of effect. Overall these studies suggest that REM sleep may have a role in the brain's preparation for (Lewin & Glaubman, 1975), and processing of, divergent thinking and cognitive flexibility tasks.

There is some evidence that the brain is primed towards an increased strength of weak associations during REM sleep. Stickgold et al., (1999) found subjects awakened from REM sleep demonstrate a pattern of priming whereby weak primes (thief-wrong) lead to greater priming than strong primes (hot-cold)--the contrary of what is normally observed in either the waking state or NREM sleep. Similarity, Walker et al. (2002) found that participants awakened from REM sleep solved more anagrams than did participants awakened from NREM sleep. While it is not clear what neurophysiological mechanisms may underlie this bias towards weak associations in REM sleep, it has been suggested that low aminergic levels characterizing this state may account for the effect. Performance on tests measuring cognitive flexibility, including anagrams, is improved following b-adrenergic blockade with propranolol and reduced following the administration of the adrenergic agonist ephedrine (Beversdorf et al. 1999).

REM sleep is also reliably associated with emotional materials. This effect was found for emotional pictures (Nishida et al., 2009), emotional stories (Tilley and Empson, 1978. Wagner et al., 2001) emotional films (Baekland et al., 1968; Goodenough et al., 1975), the recall of adjectives indicative of personal dissatisfaction (Cartwright et al., 1975) and threatening social interactions (Cohen, 1975). The unique neurophysiology of REM sleep, namely the increased activity in cortical theta, elevated acetylcholine levels and increased amygdala activity, may implicate this stage of sleep in emotional memory processing (Walker, 2009; Walker & van der Helm, 2009). Moreover, REM sleep is characterized by the co-activation of the hippocampus and the amygdala, which become synchronized in the theta activity band of the EEG (Pare & Gaudreau, 1996; Hegde et al.,

2008; Karashima et al., 2010). Because emotional memory formation in the waking state involves such co-activation (Hamann et al., 1999; Canli et al., 2000; Dolcos et al., 2004) and theta-band synchronization (Seidenbecher et al., 2003; Pape et al., 2005), a similar relationship in REM sleep may underlie this stage's association with emotional declarative memory processing.

A third trend relates to Smith et al.'s (2004) proposal that REM sleep is associated with complex procedural tasks whereas Stage 2 sleep is involved in the refinement of simple and or existing procedural skills. Accordingly, REM sleep was associated with novel complex motor learning, i.e., trampolining (Buchegger et al., 1988; 1991), the pursuit rotor task (Peters et al., 2007; Plihal and Born 1997), and complex cognitive procedural tasks, namely the Wff'n Proof complex logic task (Smith 1993, Smith & Lapp, 1986, Smith & Weeden, 1990), the tower of Hanoi (Smith 1995; 2004), the Wechsler Adult Intelligence Scale (Fienberg et al., 1973) and adaptation to inverted lenses (DeKoninck & Prevost, 1991; DeKoninck et al., 1996).

Complex declarative learning is also associated with REM sleep; tasks such as learning Morse code (Guerrein et al., 1989; Mandai et al., 1989), intensively learning French (DeKoninck et al., 1989), and learning meaningless sentences and anomalous prose passages (Empson & Clarke, 1970). The association of declarative tasks with REM sleep is at odds with the 'dual-process hypothesis' that posits that this stage is associated with non-declarative tasks that are independent of the hippocampus. The association of REM sleep with learning stories (Empson et al., 1980) and an episodic-like memory task (Rauchs et al., 2004) further argues against the 'dual-process hypothesis'. It is also of note that only two studies have examined episodic-like memory. In contrast, numerous studies have demonstrated that REM sleep is not involved in learning simple declarative tasks (see table 2).

That REM sleep is involved in divergent thinking, cognitive flexibility and the processing of emotional memories fits well with the notion that dreams are bizarre and emotional. Indeed, dreams are known for mixing loosely related elements together in a single scene (Freud, 1900) that can sometimes lead to creativity. Indeed, several scientific

and artistic achievements are attributed to dreams (Maquet & Ruby, 2004) and feature examples of divergent thinking. Dreams are also known for their emotional, often dramatic qualities (Freud, 1900). However, it is not known if REM sleep dreaming is associated with the instigation of cognitive flexibility and divergent thinking or the improved learning of emotional materials. Nevertheless, studies that have taken into account dreaming have found a relationship between the presence of task-related elements in dreaming and language acquisition (DeKoninck et al., 1989) and adapting to inverted lenses (DeKoninck & Prevost, 1991; DeKoninck et al., 1996). Two additional studies not previously reviewed also suggest a link between dreaming and memory processes. First, Cipolli et al. (2005) found that dream elements that are interrelated are better remembered in a surprise morning recall task. Second, stories learned before sleep are better recalled the next day when elements of the story are incorporated in a dream (Fiss et al., 1977).

Table 2. Summary of studies that have examined REM sleep in relation to memory and cognition in humans.

	Studies indicating a role for REM sleep	**Studies indicating no role for REM sleep**
Declarative tasks		
Divergent thinking and cognitive flexibility	Guilford's utility task • Lewin & Glaubman, 1975 Anagram solutions • Greiser et al., 1972 • Scrima, 1982 Task designed to elicit curiosity, emotions and divergent thinking • Lewin & Gombosh, 1973 Thematic apperception test solutions • Cartwright, 1974 Remote-associates task • Cai et al., 2009	Remote-associates task • Cartwright, 1974
Emotional declarative	Adjectives indicative of personal dissatisfaction • Cartwright et al., 1975 Emotional stories • Tilley and Empson, 1978 • Wagner et al., 2001 Anxiety arousing film • Baekland et al., 1968	

	• Goodenough et al., 1975 Threatening social interactions, • Cohen, 1975 Emotional pictures • Nishida et al., 2009	
Declarative word tasks	Word pair associates • Fogel et al., 2007	Guilford's word fluency task • Lewin & Glaubman, 1975 Trigrams • Chernik, 1972 • Castalda et al., 1974 • Scrima, 1982 Verbal paired associates • Castaldo et al., 1974 • Chernik, 1972 • Ekstrand, 1972 • Ekstrand et al., 1971 • Lewin & Glaubmann, 1975 • Smith, 1993 • Plihal and Born, 1997 • Genzel et al., 2010 • Rasch et al. 2009 Serial or clustering verbal memory • Lewin & Glaubman, 1975 Serial word lists • Empson & Clarke, 1970 • Castaldo 1974, experiment 1 • Bertini & Torre, 1973 • Yaroush et al., 1971 • Fowler et al., 1973 Word recognition task • Smith, 1995 Crossword puzzles • Cartwright, 1974
Declarative anomalous word tasks	Meaningless sentences and anomalous prose passages • Empson & Clarke, 1970	
Complex declarative tasks	Morse code • Mandai et al., 1989 • Guerrein et al., (1989) Learning French • DeKoninck et al., 1989 Exam period • Smith & Lapp, 1991 Learning stories	

	• Empson et al., 1980	
Episodic-like memory	What-When-Where Episodic task • Rauchs et al., 2004	
Procedural tasks		
Visual tasks	Visual discrimination task • Karni et al., 1994 • Stickgold et al., 2000	Visual non-verbal figure task • Smith, 1995 Visual motor • Rasch et al. (2007)
Implicit word tasks	Word fragment completion • Smith, 1995	
Implicit motor task	Serial reaction time task • Maquet et al., 2000 • Laureys et al., 2001 • Peigneux et al., 2003	
Motor tasks	Novel complex motor learning • Buchegger et al., 1988; 1991 Mirror tracing • Smith 2004 Pursuit rotor task • Peters et al., 2007 • Plihal and Born, 1997 Sequential finger-tapping task • Fischer et al., 2002 • Rasch et al., 2009	Mirror-tracing task • Tweed et al., 1999 Sequential finger-tapping task • Genzel et al., 2010 • Rasch et al., 2009
Complex logic Tasks	Wff'n Proof logic task • Smith & Lapp, 1986 • Smith, 1993 • Smith and Weeden, 1990 Tower of Hanoi • Smith 1995 • Smith 2004 Wechsler Adult Intelligence Scale • Fienberg et al., 1973	
Spatial Tasks	Corsi block tapping task • Smith, 1995	
Adaptation	Adapting to inverted lenses • DeKoninck & Prevost, 1991 • DeKoninck et al., 1996	

In sum, previous studies converge in supporting the possibility that REM sleep is involved in 1) tasks requiring divergent thinking and cognitive flexibility, 2) declarative materials that are of an emotional nature and 3) complex tasks of a motor, cognitive procedural or declarative nature. Furthermore, episodic memory has been largely neglected by studies of sleep and memory and, although preliminary evidence suggests that dreaming may be associated with adaptation and learning, very few studies have taken dreams into account.

In the following section the role of SWS, stage 2 and NREM1 in memory processing will be reviewed. Because of the focus the present dissertation is on REM sleep, other sleep stages will be reviewed only briefly.

Studies examining SWS and memory

Studies utilizing early-night/late-night paradigms have consistently associated SWS-rich early night sleep with the learning of word lists but not motor tasks (Fowler et al., 1973; Plihal & Born, 1999; Gais et al., 2002; Gais & Born, 2004), suggesting that this stage is involved in the processing of declarative but not procedural memories. However, a recent study deprived participants of SWS and found no effect on verbal paired associates (Genzel et al., 2009). This may mean that the small amount of SWS received by SWS-deprived participants was sufficient for the consolidation of simple declarative memory. In addition to simple declarative tasks, SWS is also associated with spatial tasks (Plihal & Born, 1999; Peigneux et al., 2004), which can also be considered as declarative in nature. Early night sleep has also been linked to autonoetic awareness during the recall of word lists (Drosopoulos et al, 2005; Daurat et al., 2007).

Recent studies have provided evidence consistent with the notion that the cortical slow wave and hippocampal ripple activity characterizing SWS sleep support the reactivation of declarative memory traces and facilitate their integration within neocortical areas (Diekelmann & Born, 2010). Evidence that slow oscillations are causal to declarative memory consolidation was found in a study by Marshall et al. (2004) in which increasing the magnitude of slow oscillations with transcranial direct current stimulation during SWS

facilitated the recall of word-pairs learned before sleep, but did not affect procedural motor tasks. That the reactivation of memory traces occurs during SWS is suggested by the finding that sleep-dependent learning of a spatial task is associated with hippocampal reactivation during SWS (Peigneux et al., 2004). Using a "cue dependent recall" paradigm, two studies have demonstrated that memory processing or "reactivation" relating to specific tasks can be triggered during SWS. Rasch et al. (2007) demonstrated that presenting a task-associated odor during SWS, but not during REM sleep, improved the consolidation of visual paired associate stimuli. Rudoy et al., (2009) played unique sounds during the presentation of individual objects in an object-location associations task. Memory for object locations was improved after sleep for objects whose associated sound was played during SWS, and not REM sleep. These results suggest that a selective reactivation of individual memory items can occur during SWS sleep and lead to their consolidation.

In the context of the standard model of memory (Squire, 1986; 2004), it is argued that the reactivation observed in these studies underlies the transfer of memory traces from the hippocampus to diffuse neocortical areas (Diekelmann & Born, 2010). In rodents, hippocampal reactivation of pre-sleep exploratory behavior is observed at the cellular level during SWS (Wilson & McNaughton, 1994; Lee & Wilson, 2002; Ji & Wilson, 2007) and is paralleled by replay in neocortical areas such as the prefrontal (Peyrache et al., 2009), parietal (Qin et al., 1997) and visual (Ji & Wilson, 2007) cortex. This hippocampal reactivation occurs in conjunction with sharp wave ripples (Wilson & McNaughton, 1994; Molle et al., 2006; Peyrache et al., 2009) which have been associated with learning (Ego-Stengel & Wilson, 2009; Girardeau et al., 2009; Ramadan et al., 2009) and which may promote synaptic potentiation (Bramham & Srebro, 1989). Together these findings suggest that SWS sleep is ideally suited for processing declarative memories and integrating them within neocortical areas (Diekelmann & Born, 2010). Moreover, it is believed that the transfer and integration of memory traces from the hippocampus to neocortical networks may result in the reorganization of memory information (Sirota et al., 2003; Steriade, 2006). The association between SWS and gaining insight from hidden regularities in the

number reduction task (Yordanova et al., 2008, 2009; 2010) may lie in this reorganization of memory (Walker, 2009).

Several studies have linked procedural learning to SWS. Sleep dependent improvement of the texture discrimination task was found to be strongly correlated with SWS in the first quarter of the night and REM sleep in the last quarter of the night (Stickgold et al., 2000). Aeschbach et al. (2008) found the same task impaired by a sound stimulation-induced decrease in the amount of slow wave activity in SWS by 30 %. Huber et al. (2004) found a correlation between sleep-related improvements in a visual-motor adaptation task and local increase in slow wave activity the right parietal cortical area involved in the task. Sleep-dependent learning in this same visual-motor adaptation task was diminished by a decrease in the amount of slow wave activity induced by sound stimulation (Landsness et al., 2009).

In summary, the studies reviewed here suggest that SWS is involved in simple declarative memory, spatial learning, insight into hidden regularities and procedural learning of visual-discrimination and visual-motor tasks.

Studies examining stage 2 and memory

Studies examining a role for stage 2 in memory have found that overnight improvement on a motor sequence learning task is correlated with the amount of stage 2 sleep (Fogel et al., 2007; Morin at al., 2008; Tucker & Fishbein, 2009; Walker et al., 2002, 2003). The relationship between the amount of stage 2 and learning was found to be stronger late night than for early night stage 2 sleep for both a motor sequence task (Walker et al., 2002; 2003) and the pursuit rotor task (Fogel et al., 2007). Similarly, stage 2 sleep deprivation was found to reduce sleep-related learning of the pursuit rotor task (Smith & Fazekas, 1997) and a simple tracing task (Tweed et al., 1999); these same tasks were not disrupted by REM sleep deprivation.

Spindles are closely associated with the sleep-dependent learning of motor tasks. An increase in spindle activity was found in relationship to sleep-related improvements of the motor sequence learning task (Morin at al., 2008; Nishida and Walker, 2007; Tucker &

Fishbein, 2009) and a mirror tracing task (Tamaki et al. 2008). Increased spindle activity was also observed as a consequence of training in a variety of procedural tasks (Fogel and Smith, 2006) and more selectively, the pursuit rotor task (Fogel, et al., 2007), where sigma power increased in the second half of the night as the result of training. In a second study using the pursuit rotor task, sleep-related gains in performance were associated with spindle activity in high performers only. Spindle activity also increased after learning a new visual-motor skill (Tamaki et al., 2009).

Declarative memory improvements may also be associated with sleep spindles as suggested by studies finding increased spindle activity in relation to successful learning of paired-associates (Clemens et al. 2005; Gais et al., 2002; Schabus et al., 2004; 2008). The mechanism by which sleep spindles consolidate memory likely involves neural plasticity (Steriade, 1999) as suggested by a large influx of calcium ions into cortical cells (Sejnowski & Destexhe, 2000), an established mechanism for plasticity (Ghosh & Greenberg, 1995).

In sum, stage 2 sleep and spindle activity are reliably associated with motor tasks and, to a lesser extent, simple declarative learning.

Studies examining NREM1 and memory

NREM1 sleep has received very little attention in terms of its relationship to memory processing. In the only study directly addressing this question, Lahl et al. (2008) found that free recall of a list of 30 words was improved following either 5- to 6-minute daytime naps or a 60 min interval consisting of daytime napping but not waking activity. Another study found evidence that dreaming of a spatial task during sleep onset was associated with increased sleep-related consolidation of this task (Wamsley et al., 2010).

Summary of the sleep and memory research

The studies reviewed here describe a complex relationship between the five stages of sleep and the several types of memory that have been investigated (see table 3). Examining relationships between specific types of learning and sleep stages requires more

detailed classification than the traditional procedural and declarative distinction. For declarative memory, simple learning is associated predominantly with SWS and to a lesser extent stage 2. REM sleep seems to have a unique relationship with emotional memories and complex learning, while SWS is predominantly associated with tasks of a spatial nature. REM sleep is strongly associated with cognitive procedural tasks and those involving divergent thinking and cognitive flexibility. Motor tasks are associated with Stage 2 and REM sleep, and whether the task calls for learning new skills or the refinement of existing skills may determine whether its consolidation is determined by REM sleep or Stage 2, respectively (Smith et al., 2004).

Table 3. Relationships between sleep stages and classes of learning. Bold "X" indicates exclusive relationships between a sleep stage and a type of learning.

	S1	S2	SWS	REM
Declarative	x	x	x	x
Simple	x	x	x	
Complex				**X**
Emotional				**X**
Spatial			**X**	
Procedural		x	x	x
Motor		x		x
Cognitive procedural				**X**
Cognitive Flexibility				**X**

Sleep-dependent consolidation has been linked to particular sleep phenomena such as spindles or theta and sigma band activity. While these phenomena are associated with a particular sleep stage, they are also found at times in adjacent sleep stages. Studies show that several stages of sleep can contribute to a task, such as Stickgold et al., (2000) who found that REM sleep in the fourth quarter of the night and SWS in the first quarter of the night both strongly correlated with learning on the visual discrimination task. While

numerous studies have examined semantic and motor memory in relation to SWS, REM sleep and stage 2 sleep, there is an important lack of studies examining episodic memory and NREM1 sleep. Indeed, one study has examined episodic-like memory in relation to sleep (Rauche et al., 2004) while only two other studies examined autonoetic awareness and sleep (Daurat et al., 2007; Drosopoulos et al., 2005). Only 2 studies have investigated NREM1 sleep in relation to learning (Lahl et al., 2008; Wamsley et al., 2010). The role of dreaming in memory processing has also received little attention even though a relationship between dreaming and learning was found in all previously mentioned studies that examined sleep mentation (DeKoninck et al., 1989; DeKoninck & Prevost, 1991; DeKoninck et al., 1996; Fiss et al., 1977; Wamsley et al. 2010).

In sum, it is becoming increasingly clear that memory depends upon sleep. The last 10 years have seen a surge in studies demonstrating a role for sleep in memory consolidation. While the joint study of sleep and memory has led to breakthroughs in both fields, such studies are also burdened by the multiple complexities inherent to both. Sleep is typically divided into 5 neurophysiologically and phenomenologically distinct stages (Hobson et al., 2000), while memory is usually divided into several memory systems and processes that are each characterized by unique phenomenologies and neural substrates (Tulving, 2002). Numerous studies have demonstrated that distinct stages of sleep are associated with distinct types of memory (Smith, 2001; Rauchs et al., 2005). Much research has also shown that neurophysiological processes associated with specific sleep stages interact with the neurophysiological processes of distinct memory types (Stickgold & Walker, 2007). In contrast, there is almost no research examining how the phenomenological characteristics of different memory systems relate to the phenomenological qualities of sleep stages. The research presented in the current thesis will address this lack by jointly examining the phenomenologies of sleep and memory to help clarify still unresolved issues of sleep-dependent learning.

Sleep and Episodic Memory

With the current emphasis on phenomenology, the focus of the present thesis is on REM sleep, which is characterized by frequent and vivid dreaming, and episodic memory, which is characterized by autonoetic awareness. These share common phenomenological and neurophysiological characteristics that will be considered in relation to sleep-dependent memory consolidation. In line with a phenomenological approach, neurophysiological features of both REM sleep and episodic memory will be discussed in so far as they underlie the particular subjective experiences unique to each, i.e., of REM sleep *dreaming* and episodic memory *recall*.

Unlike the case for non-declarative or simple declarative memory, very few studies have examined the role of sleep in episodic memory. In fact, only three studies have looked at sleep-related episodic memory consolidation (Daurat et al., 2007; Drosopoulos et al., 2005; Rauchs et al., 2004). Moreover, the studies have produced conflicting results as to whether REM sleep or SWS is involved in its consolidation. In a later section I argue that the use of different measures, stemming from different conceptualizations of episodic memory across these studies, may explain these discrepant results. In order to do this, an examination of the concept of episodic memory, especially in relation to the related concept of recollection, is necessary.

Episodic memory and recollection

The conceptualization of episodic memory has evolved since Tulving introduced the term in his seminal 1972 paper, and today the term 'episodic memory' is used in at least two distinct ways by different authors. Tulving first proposed that “episodic memory stores and retrieves information about temporarily-dated episodes or events, and temporal–spatial relations among events” (Tulving, 1972, p. 385). This refers to the notion of the factual (‘what’), spatial (‘where’) and temporal (‘when’) aspects of episodic memory. In subsequent publications, Tulving (1983, 1985, 2000, 2002, 2005) places the subjective re-experiencing of events at the center of episodic memory: “[episodic memory] makes possible mental time-travel through subjective time—past, present and future. This mental

time travel allows the “owner” of the episodic memory (“self”), through the medium of autonoetic awareness, to remember one’s own previous “thought about” experiences. . .” (Tulving, 2005, p. 15). According to this view, episodic memory is the capacity to re-experience events with the 'mind's eye'.

Central to this notion of episodic memory are 1) autonoetic awareness, defined as a conscious recollection of the original events by mentally reliving them, which allows a sort of “time travel”, i.e., the ability to go back in time to re-experience events, and 2) that the re-experiencing concerns the ‘what’ ‘where’ and ‘when’ of personally experienced events. Tulving differentiates between autonoetic awareness, considered to be the “standard experiential mode of the episodic memory system” (Duzel et al., 1997, p. 5973), and noetic awareness, which is characterized by an absence of ‘re-experiencing' and is considered as the “standard experiential mode of retrieval operations in the semantic memory (general knowledge) system” (Duzel et al., 1997, p. 5973).

A common method to study the “re-experiencing” aspects of episodic memory is to use personal memories as memory items. While this method allows for high ecological validity through the utilization of real-life events, it suffers from an important lack of experimental control over the memory items.

A second, more frequently used method addresses these concerns through the use of word lists as experimental stimuli. Unlike personal memories, lexical items can be carefully controlled and standardized. One method utilizing word lists to differentiate between autonoetic and noetic responses is the 'know/remember' paradigm. Typically, the remember/know paradigm involves a first list of words that is presented and participants must make old/new judgments on a second list. In a study by Tulving and colleagues (1977), participants “were required to respond R [remember] if they could remember anything about the actual event of the word’s occurrence in the study list, re-experiencing the episode (p.5974). Thus, when presented an item, participants must indicate if they can re-experience the episode of item presentation (a “remember” response, i.e., autonoetic awareness) or if they made an old/new decision without re-experiencing the episode (a 'know' answer, i.e., noetic awareness).

However, the remember/know paradigm is more frequently used in a related but distinct way by other researchers, including Tulving himself. Notably, Yonelinas, a proponent of the dual process framework (Yonelinas, 2001) does not explicitly utilize re-experiencing as a criterion to differentiate 'know' from 'remember' responses (see table 4). Instead, a "remember" response is indicated by the recollection of qualitative details regarding the initial moment of encoding and 'known' responses are made on the basis of *familiarity* and in the absence of recollection. For example, in one study 'remember' responses are measured as the ability to accurately remember the color of the studied word (Yonelinas and Levy, 2002). 'Know responses' are considered as reflecting 'familiarity' while 'remember' responses are considered to reflect 'recollection'.

Table 4. Comparison of Tulving's and Yonelinas's conceptualizations of the know/remember paradigm.

	Yonelinas (as described in Yonelinas, 2002)	Tulving (as described in Duzel et al., 1997)
Paradigm	The Know/Remember Paradigm	The Know/Remember Paradigm
Criteria for a 'remember' response	Some amount of detail information	Re-experiencing the experimental event
Criteria for a 'know' response	Recognition & no detail information	Recognition & absence of re-experiencing
Terminology for 'remember' response	Recollection	Episodic
Terminology for 'know' response	Familiarity	Semantic

Yonelinas and Tulving thus seem to utilize the remember/know paradigm in overlapping but critically different ways. Yonelinas considers 'remember' responses as 'recollection' processes (he does not use the term 'episodic') based on a threshold retrieval

process and measured by the presence of detail information in regards to the memory item. In contrast, Tulving considers 'remember' responses as 'episodic' using the criterion of 'autonoetic awareness' that is measured by the presence of 're-experiencing' the experimental event. A major consequence of these differential uses of the know/remember paradigm concerns the criteria for a 'remember' response,'re-experiencing' is critical to Tulving while only implied for Yonelinas. For example, in a word list experiment, remembering that a word was red is sufficient for Yonelinas to consider it a 'remember ' response, while Tulving's criteria would further require the participant to report that they can re-experience the red word with their 'mind's eye'.

While a description of these two different uses of the remember/know task clarifies conceptual issues surrounding this paradigm, in reality Tulving does not always follow the criteria of his Duzel et al. (1997) publication; in fact, he (e.g., Solerlund et al 2007) sometime uses Yonelinas' recollection criterion (Yonelinas, 2002). Nonetheless, there is a clear dichotomy between the two authors: Tulving has written extensively about the central role of re-experiencing in his conceptualization of episodic memory (Tulving, 1983, 1985, 2000, 2002, 2005), while Yonelinas (2002) does not emply terms such as re-experiencing and autonoetic (both terms are absent from his lengthy 46-page review of recollection, with episodic memory only mentioned in relation to Tulving). Accordingly, Yonelinas systematically considers his work to be examining recollection and not episodic memory. Unfortunately, Tulving is not as systematic in his use of the term episodic memory; he sometimes considers remember/know studies that lack any mention of re-experiencing as examining 'episodic memory'. This obscures the definition of episodic memory: on the one hand he writes at length on the central role of re-experiencing in episodic memory, but on the other does not always consider re-experiencing as a defining feature of episodic memory (perhaps because he uses word lists as experimental stimuli). In face of this inconsistency, for the present dissertation I will refer to Tulving's conceptualization of episodic memory and the know/remember paradigm as critically dependent upon the concept of re-experiencing, as detailed in the methodology of Duzel et al. (1997), and in the spirit of his theoretical writings (Tulving, 1983, 1985, 2000, 2002, 2005).

In sum, Yonelinas and Tulving seem to be focusing on two different phenomena relating to memory. Yonelinas is interested in the threshold between familiarity (I recognize him, but who is it?) and recollection (that's Jack, the bartender at Le St-Sulpice); in contrast Tulving focuses on the threshold between semantic knowledge (Jack works at Le St-Sulpice) and re-experiencing (I can replay in my head the first time we met). Of course, recollection and re-experiencing are not mutually exclusive and often co-occur: the participant providing the above example of recollection (Jack works at Le St-Sulpice) may be re-experiencing (or not), but only Tulving's approach truly ensures us of this. Tulving's criteria, however, cannot make the distinction between familiarity (recognizing an item in the absence of detail information) and recollection (recognizing an item and its related detail information).

Because this dissertation is concerned with phenomenological aspects of memory and dreaming and in later sections will delve into concepts closely related to 're-experiencing' such as scene construction (Hassabis and Maguire, 2007) and future episodic thought (Szpunar, 2010), I will consider mainly Tulving's conceptualization of the know/remember paradigm. Accordingly, while some authors (e.g., Yonelinas, 2002) limit the remember/know paradigm to recognition memory, episodic memory as conceptualized by Tulving is clearly not restricted to recognition memory. For this reason, research presented in the dissertation will sometimes utilize cued-recall questions in regard to the remember/know paradigm, which I argue is legitimate within the context of Tulving's conceptualization of episodic memory (but would not be so within the framework utilized by Yonelinas).

In the following section, studies having examined the effect of sleep stage on episodic memories and/or recollection (Daurat et al., 2007; Drosopoulos et al., 2005; Rauchs et al., 2004) are examined in light of the distinctions made above. It is concluded that the only study finding a REM sleep-specific consolidation (Rauchs et al., 2004) is also the study with the stimulus and method that most closely approximates Tulving's notion of episodic memory.

Episodic memory consolidation in sleep

All three of the episodic/recollection memory-sleep studies used a "remember/know" paradigm in relation to memorizing word lists (Daurat et al., 2007; Drosopoulos et al., 2005; Rauchs et al., 2004). As illustrated by Table 5, the studies differ in regard to 1) whether 'remember' responses are associated with re-experiencing (Tulving's criterion) or detail information (Yonelias' criterion) and 2) the degree to which experimental events contained 'what', 'where' and 'when' information. The results of the studies also differ significantly, possibly as a consequence of these methodological differences.

Table 5. Comparison of three studies having examined episodic memory and sleep with different conceptualizations of the remember/know paradigm. Shaded cells indicate criterion that most closely approximate Tulving's conceptualization of episodic memory.

	Rauchs et al., 2004	Drosopoulos et al., 2005	Daurat et al., 2007
'What' component	14 Words	48 Words	36 Words
'Where' component	Top or bottom	--	--
'When' component	List 1 or 2	List 1 or 2	--
Remember response criteria	Re-experiencing (minimal criterion)	Detail information (list membership)	Re-experiencing (minimal criterion)
Associated sleep stage	REM	SWS	SWS

Drosopoulos et al. (2005) used 2 word lists of 24 words each in their memory task and responses were considered as 'remember' when participants could indicate in what list out of the two the word was seen. This method clearly follows Yonelinas' method and criterion for recollection. Accordingly, the authors consider 'remember' responses as indicating 'recollection' and make no explicit mention of re-experiencing or episodic

memory. The existence of two lists constitutes temporal (‘when’) information; spatial information (‘where’) is lacking in this experiment.

In contrast, a spatial component was present in a similar experiment by Rauchs et al (2004) by having participants recall word location (top vs. bottom) for stimuli consisting of two lists of seven nouns each. The experimenters also asked participants for word order (first or second list), thus in effect constituting the ‘where’, ‘when’ and ‘what’ aspects of episodic memory (Tulving, 2002). ‘Remember’ responses needed to be justified by some recollection of what had occurred when the item was encoded, that is, thoughts, feelings or perceptions. In other words, a simple thought or evoked image occurring at the time of the encoding (e.g., it made me think of…) was sufficient to characterize the memory as episodic. While this criterion does not explicitly target re-experiencing, it is much closer to Tulving's notion of episodic memory than is the criterion of the Drosopoulos et al., 2005 study (i.e., recall of word color). Also, unlike Drosopoulos et al., Rauchs et al (2004) consider their 'remember' responses to reflect autonoetic awareness and consider their study to be an investigation of episodic memory.

Daurat et al. (2007), who used two lists of 36 words each as memory items, had participants identify old and new words in a subsequent retest as in the other two studies. In a manner very similar to Rauchs et al. (2004), they controlled for “remember” responses by asking for some type of justification to ensure that participants remembered the circumstances surrounding the item’s presentation in the study list. However, unlike Rauchs et al., (2004) there was no explicit measure of the 'where' or 'when' components of episodic memory.

In sum, the three studies meet Tulving’s criteria for episodic memory to varying degrees. As illustrated in Table 5, Rauchs et al (2004) most closely approximates Tulving's conceptualization of episodic memory. This study was the only one that measured the ‘what’, ‘where’ and ‘when’ aspects of episodic memory, and in addition featured a remember/know methodology that approximates that used by Tulving to measure the presence of re-experiencing (Duzel et al., 1997) It is also the only study that found an association between REM sleep and ‘remember’ responses. In contrast, Daurat et al.

(2007) and Drosopoulos et al. (2005) found that early night sleep, which is normally rich in SWS, but not late night sleep, normally rich in REM sleep, was associated with increased number of 'remember' responses. These results fit well with the notion that simple declarative memories are associated with SWS (Gais and Born, 2004), but that complex cognitive tasks are associated with REM sleep. However, while the Rauchs et al., 2004 study more closely approximates Tulving's conceptualization of episodic memory, it still falls short of properly evaluating the re-experiencing element. Research examining episodic memories of life events use much more stringent criteria to determine if recall of an item is a 'know' (noetic) or 'remember' (autonoetic) response. Tests to measure episodic memories, such as the TEMPau task (Piolino et al., 2003), emphasize the reliving of affective-sensory-perceptual details. Other studies (unrelated to sleep) using the "know/remember" paradigm also use stringent criteria for "remember" responses. For instance, Danion et al. (2005) required that participants give details aloud to ensure that they were using 'remember' responses (presumed to reflect episodic memory) properly. An example of a "remember" response from the Danion et al study is as follows:

> *A meeting (the participant recollected very specific details of the scene, his/her feelings and thoughts) that took place in a particular environment (the participant relived the specific atmosphere, his/her position in the scene) 2 years ago (the participant recollected the thoughts he had with regard to the fact that the meeting took place exactly 5 years after his school graduation, the time of day). [p. 539]*

Furthermore, in the Danion et al study a "know" response was described as knowing what happened including the where and when of the event, but without mention of any conscious recollection.

While word lists may be particularly well suited for research examining Yonelias' conceptualization of recollection, Tulving's notion of episodic re-experiencing may be

particularly amendable to the use of real-life events as memory items. To address this issue, we utilized VR technology to achieve high levels of ecological validity, while at the same time maintaining some control over experimental items in a manner similar to word-list studies. This component of the thesis will be described in more detail in a later section.

Episodic memory recall and dreaming

In the following sections, it is suggested that parallels between dreaming and episodic memory support the possibility that the two phenomena are linked. Specifically, several lines of research converge on the notion that the hippocampus may be central to encoding contextual detail and expressing this contextual detail in both dreaming and episodic memory. The following sections review this convergence of findings.

Hippocampus and context

Authors researching the spatial and temporal functions of the hippocampus usually define context as the set of background features that surround an event. Accordingly, spatial context refers to *where* an event occurred in relation to the environment and its stimuli, while temporal context refers to *when* an event took place in relation to other events. The spatial aspect of context has been widely studied and there is clear evidence that the encoding of spatial variables is dependent on hippocampal place cells (Bostock et al., 1991; Tanila et al., 1997; Anderson and Jeffery, 2003). Similarly, temporal context is believed to be generated by the timing patterns of hippocampal cell spiking (Bower et al., 2005; Ferbinteanu and Shapiro, 2003; Shapiro and Ferbinteanu, 2006). Recent findings indicate that place cells fire in relationship to non-geometric stimuli, thus expanding the concept of context to encompass non-spatial and non-temporal elements. For example, in rats hippocampal neurons respond to changes in colors and odors associated with an environment (Anderson and Jeffery, 2003; Hayman et al., 2003). It has been recently proposed that goals also constitute an important contextual variable, as suggested by the encoding of reward in conjunction with spatial and temporal variables in the hippocampus (Smith and Mizumori, 2006a). Similarly, Tulving (1983) independently argued that goals

are fundamental to episodic memory. A term such as "situational context" may refer to aspects of context that transcend simple temporal, spatial and perceptual elements. Episodic memory recall and dreaming appear to possess contexts that concern all of these factors: a situation that unfolds in time, that describes complex relationships between items and that may be centered on motivation and goals. Descriptions of the medial temporal memory system (as first proposed by Mishkin, 1982) demonstrate the need for a concept such as situational context to account for phenomena such as episodic memory recall and dreaming.

Briefly, Mishkin's system stipulates that neocortical input arrives from two separate streams into the parahippocampal region: 1) input concerning object features ('what') converging in the perirhinal area and 2) input concerning the object location ('where') converging in the parahippocampal cortex and medial entorhinal area. The 'what' and 'where' streams then themselves converge and are bound together in the hippocampus. The resulting 'what/where' context accounts for various phenomena such as item recognition, item associations, familiarity and recollection. However, this account overlooks a fundamental aspect of episodic memory and dreaming: the 'how' and the 'why' of an event. To account for episodic memory and dreaming, the broader notion of situational context is needed. Situational context differentiates episodic memory from other types of memory processes yet is also central to the process of dreaming.

The following section will concern how the hippocampus, via situational context, encodes and permits the recall of episodic memory. Then, a similar system underlying dreaming will be examined.

Hippocampus functioning in episodic memory retrieval

According to one widely accepted perspective on episodic memory, the multiple trace theory (Nadel and Moscovitch, 1997), the hippocampus plays a predominant role in enabling the retrieval of sensory experiences. It is thought that the hippocampus extracts contextual information from incoming sensory information relayed via the sensory cortexes. This contextual information serves several purposes. First, it produces a memory

trace of the contextual information (i.e., a context memory trace) in the hippocampus (Mumby et al., 2002). Second, it is fed to the neocortex in parallel with information from primary sensory areas (Pan and Tsukada, 2006) providing the basis for encoding the event into episodic memory (Tulving, 2002). Consequently, context is encoded by the hippocampus while contents of the event per se are stored in neocortical semantic and perceptual networks.

When an episodic memory is recalled, the appropriate hippocampal context trace is purportedly activated and projected into the neocortex. Stored in the context trace are pointers to the neocortical semantic and perceptual elements required to reconstruct the event. Without the hippocampus, which provides contextual integration of neocortical memory traces (Nadel and Moscovitch, 1998), recalling episodic memories would be impossible, as is observed in patients whose hippocampal lesions have caused amnesia (Scoville and Milner, 1957; Squire, 1992).

A number of recent studies suggest that episodic memory recall and the simulation of future events (often referred to as episodic future thought) share similar neurophysiological processes (see for review Szpunar, 2010). Hassabis and Maguire (2007) suggest that all forms of fictitious representations of events, from episodic memory to spatial navigation, share common hippocampally-mediated processes that they call "scene construction". Consequently, the multiple trace theory can be applied to many forms of "scene construction", including dreaming. While fMRI studies have shown that episodic memory recall and imaging new situations share widely overlapping brain regions which include the hippocampus (Addis et al., 2009; Hassabis et al., 2007), regions that differentiate episodic recall from imagining new situations, i.e, the precuneus and the posterior cingulate cortex (Hassabis et al., 2007), show decreased activity in REM sleep (Braun et al., 197l; Maquet et al., 1996 Nofzinger et al., 1996). The posterior cingulate cortex was also found to be involved in future and past simulation of familiar, but not unfamiliar events (Szpunar et al, 2009). Therefore, REM sleep neurophysiology may be unsuited for episodic memory recall, but rather may be well suited for creating novel situations occurring in unfamiliar contexts, i.e., dreaming.

Hippocampus functioning in dreaming

In REM sleep, neurological processes underlying episodic recall are modulated to enable a different type of memory retrieval. The hippocampus is active in REM sleep, but information flow from the hippocampus to the neocortex is dramatically reduced (Buzsaki, 1996, but see Wagner et al., 2009), possibly due to high cortisol levels that inhibit the main output field of the hippocampus (the CA1 region; Payne and Nadel, 2004). Consequently, during REM sleep the neocortical elements associated with episodic memories are activated without the spatial-temporal context normally afforded by the hippocampus, leading to the activation of memory fragments in isolation of their context at the time of encoding (Payne and Nadel, 2004; Stickgold, 2002; Stickgold et al., 2001). According to Payne and Nadel (2004), the activated memory fragments are then subject to "narrative smoothing", a natural tendency of the brain to "construct narratives" from disparate information. The resulting phenomenology consists of the bizarre imagery and unusual plotlines commonly seen in REM sleep dreaming.

In contrast to the "narrative smoothing" hypothesis, it has been argued that the hippocampus plays an important role in the construction of dream imagery. Nielsen and Stenstrom (2005) review evidence that the hippocampus, via inputs from the neocortex that remain active in REM sleep, bind the disparate neocortical episodic traces into a perceptually and thematically coherent hallucinatory environment. It is suggested that a highly salient hippocampus-based context is in fact present in REM sleep dreaming (*contra* Payne and Nadel, 2004) which serves to bind the fragmentary neocortical semantic/perceptual traces into a coherent spatial-temporal dream environment as well as a situational context. Novel combinations of context traces with previously unrelated perceptual/semantic traces, now possible because of REM sleep-specific disrupted information flow from the hippocampus to the neocortex, may underlie dream imagery formation and offers an alternative model of dream production. Phenomenological examinations of REM sleep offer some support for this notion.

First, that dreams are composed from episodic neocortical traces is strongly suggested by investigations of the memory sources of dreaming. Dreams are known for featuring elements from past events, both recent and distant (Freud, 1900). While whole episodic memories are found in only 1.6 % of dreams (Fosse et al., 2003), episodic elements in dream imagery can be readily traced to past events. When prompted to make an association between elements in the dream environment and past events, a surprising number of dream elements can be traced to episodic memories. For example, the reproduction of isolated spatial or temporal features of memories occurred in 28–38% of reports in one study (Cavallero et al., 1990). In another study, 65% of dream elements were linked to features of waking events (Fosse at al., 2003). Because incorporated elements include everyday objects and situations, as well as specific features of objects (e.g., a texture), the ability to link dream stimuli to stimuli in past waking events requires considerable effort. We have observed that the ability to identify memory sources in dream imagery increases with practice.

Second, that neocortical memory sources are bound together in a manner similar to episodic memory recall to produce dreaming is suggested by that fact that both episodic memories and dreaming are coherent, structured, predominantly visual experiences that unfold in time and mimic reality. The notion that dreams are coherent and structured requires some elaboration. Recent descriptions of dreaming emphasize its realistic spatial-temporal and perceptual qualities (e.g., Revonsuo, 2000; Nielsen and Stenstrom, 2005). Dreams are also organized around salient narrative qualities and a story-like progression (Freud, 1900; Nielsen, 2000; Hobson et al., 2000). It is parsimonious to assume that the function of the hippocampus to provide a context to bind episodic memories is also the process behind the very similarly structured context and binding requirements of dreaming.

Some studies provide some empirical support for this notion that episodic recall and dreaming are based on a common mechanism. First, damage to the hippocampus causes a deficiency in both dreaming and episodic memory recall. Indeed, the finding that hippocampal lesions affect episodic memory has often been replicated (Aggleton and Brown, 1999; Tulving and Markowitsch, 1998; Vargha-Khadem et al., 1997). Although

much less studied, there is evidence that patients with hippocampal lesions report dreams that are short, stereotyped, repetitious, unemotional and lacking day-residues or symbolic elaborations (Torda, 1969). Second, temporal references identified in episodic memories and dreams follow strikingly similar temporal distributions i.e., a linear decrease with a cubic trend reflecting a disproportionately higher number of temporal references from adolescence and early adulthood as compared with adulthood and childhood (Grenier et al., 2005). Finally, research on the chronological features of incorporations of memories into dreaming suggests a hippocampal-mediated link between dreaming and learning. Briefly, the memory sources of dreams tend to come from events occurring 12 hours (day residue) and 7 days (dream-lag effect) earlier. This finding has been replicated several times by our laboratory (see Nielsen, 2004 for review). The dream-lag effect is hypothesized to reflect time-limited memory consolidation processes of the hippocampus (Nielsen and Stenstrom, 2005). Analogously, post-learning REM sleep time, including its accompanying elevated acetylcholine neurotransmitter levels is elevated for a period of 5–7 days in rats (Smith, 2003), a time scale which corresponds to observed patterns of a 7-day delay in the incorporation of stimuli into dreaming.

In sum, dreaming and episodic memory recall share a number of phenomenological and neurophysiological similarities consistent with the notion that they are closely related. In particular, they may both be dependent on the hippocampus to bind memory elements together to create contextually coherent imagery sequences and to imbue them with situational context. Time-limited incorporations of episodic memory fragments into dreaming are believed to reflect hippocampal processes and may relate to learning. In the following section, we will briefly examine how episodic memory and dreaming differ.

Differences between episodic memory recall and dreaming

While both dreams and episodic memory recall are centered around structured representations of an event unfolding in a spatial-temporal context, they differ significantly in regard to the manner in which memory traces are utilized. During episodic memory recall, a memory trace is reactivated in order to reconstruct an event that previously took

place in some if its original perceptual detail. During dreaming, elements from several different memories are combined to give rise to a new, albeit perceptually detailed, experience. Dreaming and episodic recall thus differ in the manner in which memory traces are used.

Second, as compared to episodic memory recall, dreaming is immersive in the sense that the dreamer believes the dream to be "real." In contrast to episodic memory recall—which is commonly understood to be imaginary—dreaming is typically characterized by an unawareness of its imaginary nature (e.g., Freud, 1900), even when it possesses elements that are bizarre. Despite several studies having examined the frequency and nature of bizarreness in dreaming (Cicogna et al., 2007; Hobson et al., 1987; Revonsuo and Salmivalli, 1995), it is still unclear whether dream bizarreness applies only to the dreamt environment or whether it also applies to cognition occurring during dreaming. While it is claimed that logical rigor (Hobson, 1988; Hobson et al., 2000, Hobson, 2004) and the ability for reflection (Rechtschaffen, 1978) are diminished in dreaming, others argue that few differences in cognition are found between dreaming and waking states (Kahan and LaBerge, 1997; Purcell et al., 1986). It is therefore unclear how waking state and dreaming cognition differ, although important deficits are attributed to the latter.

Summary and overview

In sum, episodic memory and dreaming share several neurophysiological and phenomenological qualities. Episodic memory recall and dreaming deal with contextualized events that are subjectively experienced from a first person perspective. The construction of these events may rely on a hippocampally-mediated process involving neocortical sensory elements that are bound within a unique spatial-temporal context. The latter is very likely dependent upon activity in the hippocampus. A major difference between dreams and episodic memory recall lies in the extent to which they reproduce or create new experiences. While episodic memory recall involves reconstructing an event with details previously experienced, dreaming draws upon multiple memory sources and loosely associated elements that are bound together to give rise to novel and often bizarre

experiences. Furthermore, unlike episodic memory recall, cognitive deficiencies are present during dreaming. However, it remains unclear whether dreaming is related to hippocampal-mediated processes, whether dreaming is involved in the processing of episodic memory, and whether dream bizarreness relates to both the dreamed environment and cognition.

These questions are addressed in the four articles presented in the current thesis. In articles I and II we used a VR task, targeted dream sampling and REM sleep deprivation to test whether dreaming and episodic memory are associated and whether episodic memory and REM sleep are associated. In article III a participant trained in introspection underwent multiple awakenings during theta bursts of NREM1 sleep with dreaming. The dreams were assessed for indications that a) hippocampal-mediated processes are present during NREM1 sleep, b) dreaming during NREM1 sleep reflects memory processing and c) dreaming involves memory elements whose sources include loosely related episodic memories. In article IV we examined what aspects of cognition are active and selectively diminished in the face of dream bizarreness. We also examined if dream bizarreness is the result of incompatibilities between memory items and their context.

Together, the studies address the lack of research on the role of sleep in the consolidation of episodic memory (articles I and II), the role of dreaming in memory consolidation and memory processing during NREM1 sleep (article III) and the nature of dream bizarreness (article IV).

CHAPTER II

Episodic memory, REM sleep and dreaming.

In articles I and II we utilize a REM sleep deprivation paradigm conjointly with a VR task to examine the relationship between episodic memory, REM sleep and dreaming. Before presenting the articles, a brief description of the central elements of the study, including REM sleep deprivation and VR technology, will be given. In addition, the rational for incorporating emotional and motivational features in the VR task is discussed.

Selective REM sleep deprivation

Selective REM sleep deprivation has been shown in numerous studies (e.g., Karni et al., 1994; Ohno et al., 2002) to significantly reduce the amount of REM sleep obtained in a night. The procedure typically consists of waking a participant shortly after the onset of each REM sleep episode and maintaining wakefulness for a short interval before letting them return to sleep. Dreams may also be collected at this time to sample intervening cognitive processes. The effects of selective REM sleep deprivation are often compared to those produced by similar interruptions of NREM sleep that are matched for time-of-night, length of interruption and other factors. Alternatively, REM sleep deprivation may be compared with an identical procedure in which participants are awakened 15-20 min after the onset of each REM sleep episode. Our laboratory has used such a procedure to successfully deprive participants of REM sleep as suggested by various physiological indications of REM sleep pressure (Nielsen et al., 2005). In the current study, such a deprivation procedure will be used to examine the role of REM sleep and dreaming in the consolidation of episodic memory. Because both the incorporation of episodic memory fragments into dream content and the consolidation of episodic memories is thought to be dependent on REM sleep processes (see earlier), REM sleep deprivation is expected to decrease both dream incorporations of a memory task and accuracy of recall of this memory task.

Virtual reality and measures of episodic memory

Much like the studies of episodic memory reviewed earlier indicate, poor ecological validity is a problem for many types of psychological and neuropsychological tests (Bennett, 2001; Gioia and Isquith, 2004). It has been suggested that poor ecological validity is often due to the fact that tests do not visually represent the real-life situations faced by individuals and, as a consequence, do not predict real-world functioning (Schultheis et al., 2002). VR technologies have been proposed as an experimental tool to address this issue (e.g., Burgess et al., 2001). A typical VR configuration consists of an interface that allows an individual to navigate and interact with a three dimensional computer-generated audiovisual environment that mimics reality. The interface most often consists of a head mounted display (HMD), which produces a first-person visual perspective, a head position tracker to map real-to-virtual head movements within the computer-generated environment, and a hand-manipulated control (e.g., joystick or computer mouse) to control the direction of movements within the environment. Together these components maximize the participant's sense of immersion within the virtual environment and thus, presumably, to draw heavily upon episodic memory systems.

The ability of VR technologies to allow experimenters to create life-like situations makes them ideal for the study of episodic memory. In fact, VR has been used to examine the neural correlates of episodic memory (Burgess et al., 2001; King et al., 2005); the construct and ecological validities of VR stimuli for assessing memory and learning have been demonstrated in assessments of mnemonic deficits among traumatically brain-injured individuals (Matheis et al., 2007).

The current study will similarly employ VR to assess episodic memory by creating stimuli that are rich in temporal, spatial and situational context, and that emulate life-like experiences. The stimuli will be experienced from a first person perspective and will presumably engage the episodic memory system selectively.

Emotion and motivation in dreaming and its role in episodic memory consolidation

In a review of episodic memory, Conway (2003) remarks that within a short interval of as little as 24 hours many episodic memories are no longer accessible. Indeed, we can remember many details from events in our day, but only a small number of these memories survive until the next morning. Conway (2003) proposes that goal-oriented episodic memories, in particular those corresponding to our current goals, are the ones whose ability to recall we maintain over 24 hours. Emotions are also known to enhance memory for events (Ochnser, 2000; Sharot et al., 2004). In light of new research on sleep-related memory consolidation, Conway's question of "what types of episodic memories survive 24 hours" could also be read as "what types of episodic memories are consolidated by a night of sleep". Interestingly, much research indicates that REM sleep dreams are both goal-oriented and emotional in nature (e.g., Smith et al., 2004).

Some evidence supports the possibility that the episodic memory fragments containing emotional qualities 1) are more likely to be incorporated in dreaming and 2) receive greater sleep-dependent consolidation. First, it has been known since Freud (1900) that dreams deal with the emotional and motivational aspects of one's daily life. This fact has also been demonstrated by a limited number of empirical investigations (e.g., Nikles, et al., 1998; Smith et al., 2004).

Second, the recent finding (Sharot et al., 2007) that episodic-like recollection, and not familiarity, is enhanced by emotional content, and this only after a 24-hour but not a 5-min delay, supports the notion that an emotional event is consolidated by sleep. The finding that consolidation of emotional stories is dependent upon REM sleep (Wagner et al., 2001) further specifies that it is REM sleep that is involved in this function.

To test this notion, i.e., that REM sleep and dreaming mediate the emotional facilitation of episodic memory consolidation, some VR elements in the experimental stimulus were designed to evoke emotional reactions while other, matched elements were kept emotionally neutral. Subjects were subsequently tested for both episodic memory recall and dream references to the memory task for emotional and neutral memory elements separately.

In line with Conway's (2005) suggestion that goal-related events are preferentially consolidated over time, the VR stimulus in the present experiment is a goal-oriented task, i.e., it requires participants to actively search for specific locations and objects. It is expected that the presence of goal-orientation will contribute to enriching the situational context of the VR task and thus rendering the experience more conducive to both accurate recall and dream incorporation.

Procedures

As the studies' procedures are described in detail in the following article, they will be mentioned here only briefly and primarily with respect to the VR task. There were two VR two tasks, an emotional and a neutral task, and each consisted of navigating towns in search of indoor locations. Each task featured a town within which there were four target houses. Each house contained a single room in which target and incidental items could easily be found. Target items were: a table, an object (on the table) and a character. Incidental items were: a piece of furniture, an object on the furniture, an object on the wall, a fireplace and a carpet. Incidental items consisted of objects that participants did not know would be included in the recall questionnaire but whose presence was entirely appropriate to the décor of the room, e.g., furniture or paintings. The items were included in the recall questionnaire as an exploratory measure of whether the participant's "intent to remember" would differentially modulate the nature of the sleep-dependent consolidation. This measure is exploratory and not elaborated further here.

With the help of a compass that directed them toward their target destinations, participants were instructed to find each house in a particular order. Upon entering a house they were required to listen to the residing character and pick up the target object on the table. The task was part of a story identical for each participant that unfolded as he/she visited new houses, spoke to new characters and viewed new events. Locations in the emotional task contained emotional characters, emotional dialogue, emotional events, and an emotional storyline as compared to the neutral task. The objects and characters of the neutral task are presented in Appendix I, and those of the emotional task in Appendix II.

The spatial layouts of the rooms are presented in Appendix III. As can be seen in these Appendixes, the items involved in later recall were systematically distributed across both locations and tasks.

Participants were randomly assigned to CTL or REMD groups upon arriving at the laboratory. They underwent awakenings from REM sleep after which dream reports were collected. They also kept dream logs for a duration of one week after their stay at the laboratory. For both laboratory and home dream collections, participants were specifically asked to rate the degree to which the VR task was incorporated within their dreams.

Two days after the VR task participants were emailed a questionnaire measuring recall and autonoetic aspects of the factual/perceptual, spatial and temporal features of the VR task (see Appendix VI for an example). Ten to twelve days after the VR task participants returned to the laboratory to hand in their dream diaries, to undergo an evaluation of their memory of the virtual towns, and to receive a debriefing. The latter task only evaluated one component of episodic memory and was separated from the episodic task by approximately 8 days; it contained a distinct set of findings that are presented in a separate article (article II).

We hypothesized that REM sleep deprivation would disrupt the consolidation of temporal and spatial features of episodic memory as well as memory for items in emotional locations. We also expected to find a correlation between dreaming of the task and later recall.

Article I- Sleep-dependent consolidation of episodic memory following REM sleep deprivation

Author Contributions

PS and TN conceived and designed the experiment and wrote the paper. PS performed the experiment and PS and ES analyzed the data.

Sleep-dependent consolidation of episodic memory following REM sleep deprivation

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Through episodic memory we can relive moments of our lives in some perceptual detail. Studies examining the effect of sleep on this complex type of memory have used word lists as an experimental paradigm and report conflicting results concerning whether REM sleep or SWS are associated with its consolidation in long-term storage. As compared to word lists, everyday episodic memory concerns a wealth of perceptual details within a rich spatial-temporal context. Moreover, episodic memories are sometimes emotional and often implicate items that are not the object of intentional encoding. Finally, episodic memories, but not words, are readily incorporated into dreaming. Here we use REM sleep deprivation in conjunction with a virtual reality stimulus to explore the role of sleep on these facets of episodic memory. Participants navigated a realistic virtual town in search of items in target locations that varied in their emotional load (low vs. high). Items varied in whether participants were instructed to pay attention to them or not (target items vs. incidental items). Post-task sleep was manipulated to reduce REM sleep in half of the participants. Memory of the perceptual details, spatial locations and temporal order of the virtual reality items was measured two days later, while incorporation of the task into REM sleep dream content was evaluated by means of mentation interviews after laboratory REM sleep awakenings and home dream logs. Spatial memory for incidental items, but not target items, was negatively affected by REM sleep deprivation. In contrast, REM sleep deprivation was associated with better memory for perceptual details of target items but not incidental items. SWS, which was increased by REM sleep deprivation, correlated with memory for perceptual details of target but not incidental items. Autonoetic awareness, i.e., the ability to relive the event with the "mind's eye", was strongly correlated with Stage 2 in the last third of the night. Dreaming of the task during days proximal to the memory task was associated with improved recall of spatial aspects of the stimulus. Together, the findings support the notion that the main components of episodic memory are differently processed during sleep.

Introduction

Episodic memory allows us to relive events with some of their original perceptual detail and, in this sense, to "travel back in time" (Tulving, 1983). It is an inherently complex form of memory—even the simple recollection of the first catch on fishing trip contains a rich web of associations linking people, settings and objects within a distinct spatiotemporal and situational context. The mechanisms by which some events of our daily lives are selected and processed so that they remain accessible for episodic replay are largely unknown, although attentional and emotional factors are known to play important roles (Conway, 2009). The notion that sleep may be involved in episodic memory formation has been bolstered by evidence that episodic recall is improved by a night of sleep (Aly and Moscovitch, 2010). It is well established that specific stages of sleep are beneficial - and sometime critical - to the consolidation of certain types of memory (Walker and Stickgold, 2006). However, attempts to link episodic memory consolidation with specific sleep stages have yielded inconsistent results. One study showed an association between episodic memory and SWS (Daurat, Terrier, Foret and Tiberge, 2007); another an association with REM sleep (Rauchs, Bertran, Guillery-Girard, Desgranges, Kerrouche, Denise, Foret and Eustache, 2004). These discrepant results may reflect differences in the manner with which each study measured episodic memory.

At its most basic level, episodic memory is defined by the "what" (factual/perceptual information), "where" (spatial information) and "when" (temporal information) of an event (Tulving, 2002). A second defining feature of episodic memory is 'autonoetic' awareness at the time it is remembered, i.e., the ability to 'travel through time' to relive an event as opposed to simply knowing that the event happened. Studies examining relationships between episodic memory and sleep stages have measured autonoetic awareness with "remember-know" measures (Gardiner, Ramponi and Richardson-Klavehn, 2002). Briefly, a "remember" response, signifying the presence of autonoetic awareness, occurs if the recogniton of an item is accompanied by the recall of the context in which it was encoded. A "know" response is associated with the recognition of an item based on its familiarity but in the absence of recalled context.

While these studies have used similar methods to measure autonoetic awareness, the extent to which they measured the "what, where and when" components of episodic memory differ and may explain their discrepant results. In the study that found a SWS association

(Daurat et al., 2007), episodic memory was measured using simple word lists, and thus contained factual information (the identity of word) but not explicit spatial or temporal information. In contrast, Rauchs and colleagues (2004) utilized the "What-Where-When" task (Guillery, 2000) that makes use of two lists of words that differ in both spatial location (lower vs. upper) and temporal order (first vs. second) in addition to the usual factual information (identity of the word). Interestingly, the later study found a REM sleep association that was specific to spatial and temporal aspects of the task. Although compared to everyday events word lists are typically impoverished in their contextual and perceptual detail, these findings suggest that imbuing a word list with minimal spatial-temporal context shifts its dependence on SWS to dependence on REM sleep. A proper understanding of the role of sleep in everyday episodic memory therefore requires an ecologically valid measure of episodic memory.

In the present study, a realistic VR task ensured that participants experienced events and objects that were rich in perceptual detail and embedded in a contextually appropriate narrative. Participants navigated a life-like virtual town in search of interior locations that contained characters and objects to collect. Reasons for visiting locations were driven by a simple story whose development was furthered through interactions with virtual characters.

Emotions and episodic memory

There is strong evidence that emotions enhance episodic memory and may be a critical aspect in determining which experiences can be retrieved after long periods of time (Dere, Pause and Pietrowsky, 2010). In contrast to most declarative memory tasks, which involve SWS (Diekelmann and Born, 2010), the consolidation of emotional stories (Wagner, Gais and Born, 2001) and emotional pictures (Nishida, Pearsall, Buckner and Walker, 2009) are associated with REM sleep. REM sleep is characterized by features that may predispose it to processing emotional declarative memories, namely high levels of acetylcholine and increased amygdalar activation (Walker, 2009; Walker and van der Helm, 2009). However, the role of REM sleep in emotional episodic memory consolidation remains unclear. To clarify this role, we designed two version of the VR task that differed in emotional content (low vs. high) while being carefully matched for other visual and auditory details such as location and character appearance, navigational demands, etc.

Intention to remember and episodic memory

Episodic memories are formed in a mostly non-conscious and unintentional manner (Conway, 2009), which contrasts with the attentive, intentional encoding that takes place when memorizing memory items. Much evidence suggests that manipulating participants' intention to remember modulates encoding of the memory (Block, 2009). While the modulating effect of one's *intention to remember* has not been investigated in relation to sleep, one study found that the awareness of learning a motor skill is critical to its sleep-dependent improvement, suggesting that intention may modulate sleep benefits (Robertson, Pascual-Leone and Press, 2004). To investigate this question, we manipulated the participants' intention to remember specific objects by asking them to remember some objects in each room (*target items*; e.g., table, object on table, character) while objects unrelated to the task were also situated in the same room (*incidental items*; e.g., fireplace, painting). Incidental items were located inconspicuously in rooms as not to arouse suspicions that they could be the object of a surprise test. While many episodic memories that are selected for long-term storage are often not intentionally encoded (Conway, 2009), the available evidence indicates that intentional learning benefits from sleep (Robertson et al., 2004).

Dreaming and episodic memory

Recent research suggests that dreaming of a spatial task is associated with increased performance on that task (Wamsley, Tucker, Payne, Benavides and Stickgold, 2010). However, the relationship between dreaming and episodic memory is unique. On the one hand, the replay of whole episodic memories during dreaming is exceedingly rare, i.e., in 1-2% of dreams (Fosse, Fosse, Hobson and Stickgold, 2003). On the other hand, the objects, settings, characters and situations found in dreams can readily be traced to specific episodic memories (Nielsen and Stenstrom, 2005). It is thus of interest to determine whether the association between dreaming about features of a memory task and subsequent performance on that task is specific to spatial aspects of the task or extends to its temporal and factual/perceptual aspects as well. We used the life-like events of our VR memory task to examine relationships between sleep-related consolidation of episodic memory and its incorporation in dreaming.

In sum, the current study employed a realistic VR task in conjunction with a REM sleep deprivation procedure and the collection of dream reports to 1) overcome limitations in ecological validity associated with word lists; 2) independently manipulate variables that are known to modulate encoding and recall/recognition, namely, the emotional salience of item locations and the participant's intention to remember; and 3) examine relationships between task performance and incorporation of task features into dreaming. The specific hypotheses of the study were:

H1) REM sleep deprivation will disrupt spatial and temporal aspects of episodic memory performance.
H2) REM sleep deprivation will disrupt the memory of emotional task elements to a greater extent than the memory of low-emotion task elements.
H3) REM sleep deprivation-induced deficits (H1 & H2) will be observed for target but not incidental items.
H4) Dreaming of the memory task will be associated with higher performance on the episodic task.

Methods

Participants

Sixteen self-reported healthy participants (3 males, mean 25.1±5.71 years) took part in the study. They reported being free of sleep and dreaming problems, substance use including smoking, and medical and mental disorders. The study was approved by the ethics committee of Hôpital du Sacré-Cœur de Montréal. All participants gave informed consent. Two participants experienced discomfort during VR immersion and only completed the low-emotion version of the task as well as the home dream log; they were thus included only in analyses concerning dreaming. A third participant failed to complete the episodic memory questionnaire and was therefore excluded from ANOVA analyses concerning episodic memory.

Procedures

Participants arrived at the laboratory in the evening and were instructed on how to use the VR equipment and complete the VR task. After completing each version of the VR, they completed questionnaires about sense of presence and cyber sickness symptoms during their VR immersion. Once both versions of the task were completed, participants had scalp electrodes attached and the concept of autonoetic awareness and "know" and "remember" responses were thoroughly explained according to the criteria established in Duzel et al. (1997). In brief, participants were instructed to report "remember" responses if they could 'see' the event involving the memory item in their "mind's eye", and to report "know" responses if they knew the answer but could not visualize the event involving the memory item.

One hour before sleep, participants completed a practice episodic memory questionnaire on a laboratory computer. They were then randomly assigned to either a REM sleep deprivation (REMD) or a control (CTL) condition and slept in the laboratory. After the final morning awakening, electrodes were removed and the use of the dream log was explained. Participants were told to expect a questionnaire by email the following day and that its prompt and thorough completion was extremely important. Participants were then free to leave the laboratory. Two days after the VR task, they received the questionnaires by email and returned them once completed. Additional questionnaires were emailed and completed 5 and 8 days following the VR task, but findings are not presented here. Between 9 and 11 days after the VR task, participants returned to the laboratory to hand in their dream logs and to complete additional tasks not presented here. They were debriefed and compensated 75$ for their participation.

The VR Task

The two versions of the VR task were programmed with the "TES construction kit" (Bethesda Softworks) and utilized the "Elders Scrolls IV: Oblivion" 3D engine (Bethesda Softworks) running on a HP XW4600 computer (Dual Core E6850, 3.00GHz, 4 GB RAM, NVIDIA GeForce 8800GTX video card). The VR environment was navigated from a first person perspective via a head-mounted display (eMAGIN Z800 3DVisor at 1024x768 resolution) and a virtual compass at the bottom of the screen indicating the relative direction to their target location. A wireless mouse was used for initiation of movement (left click =

forward) and interactions with the VR environment (right click = pick up object, open doors, initiate conversation). Surround sound was provided by a Sony Home theater 6.1 channel system.

The two versions of the VR task each lasted approximately 25 minutes, and featured separate towns and stories. As shown in Figure 1, the two virtual towns were similar except for the fact that one was designed to be emotional arousing (high emotion task), and the other to be minimally emotional (low emotion task). In both cases, the principal objective was to locate an introductory character located at the outskirts of the town. Clicking on the character triggered an in-game animation during which the character looked at and spoke directly to the participant and the participant could not move his/her virtual "body". This dialogue, lasting approximately 2 minutes, engaged the participant in development of the story, for example, at the onset, the participant was informed of the first target indoor location and how it related to the scenario.

Each virtual town featured 4 target indoor locations attainable only through a door that contained a single room housing 2 target items, i.e., a character and an object on a table (see Figure 2 for an example). Also present were several incidental objects: 1 piece of furniture (other than a table), 1 object resting on the piece of furniture, one object leaning against the piece of furniture, one object hanging on a wall (e.g., painting), 1 fireplace and a carpet. Other non-target buildings had locked doors and could not be entered. When entering a house, participants had been previously instructed to engage the character in dialogue and to pick up a target object resting on a table. Clicking on the character triggered a monologue lasting approximately 20 seconds and advanced the story while informing participants of their next target location.

In the high emotion version of the task an emotionally arousing event took place in each location (e.g., character getting murdered) and sinister music played at low volume as long as participants remained there. Characters were in visibly and audibly negative moods (e.g., angry, worried or annoyed) and the story itself was emotion-provoking (a series of murders and arrests resulting from a corrupt official's actions). In contrast, in the low-emotion version of the task the story line was emotionally mild but entertaining (a "who-done-it" mystery concerning a stolen painting) and involved characters in generally neutral or positive moods. Pleasant music played in each low emotion location and no emotionally negative events occurred at any point. All 8 locations (4 low emotion, 4 high emotion) were

matched for size and positioning of items and characters. Characteristics of items (e.g., color) and of characters (e.g., hair length, color) were systematically counterbalanced across locations.

While participants could navigate and explore the virtual locations freely, they experienced essentially the same contexts, events and experimental stimuli by virtue of being directed by the compass, the unidirectional story line, scripted dialogues, participant-triggered events and obligatory viewing of events and character dialogues. Importantly, all target items on the subsequent memory test required a participant interaction, thus ensuring that participants spent similar amounts of time attending to the items.

Each participant's progress through the VR scenario was tracked by the experimenter on a computer monitor in an adjacent control room; this ensured that instructions were followed and allowed the experimenter to end the task when all 4 objects had been collected. Participants took a short break (10 minutes) between the two versions of the task and filled out questionnaires about cybersickness symptoms and sense of presence during VR immersion. The order of the two versions of the task was counterbalanced across participants.

REMD procedures

Participants slept in a sound isolated, electrically shielded room containing a single bed. A video camera, microphone, and intercom system were used to maintain visual and voice contact at all times and were used to record dream mentation reports. Sleep stages were recorded with an electrode montage of 19 standard 10-20 system electroencephalogram (EEG) channels, 4 electrooculogram (EOG) channels (left/right, vertical/horizontal), and 1 electromyogram (EMG) channel (submental). All-night recordings were achieved using a Grass Model 12 Neurodata Acquisition System (-6 dB filters with cutoffs at 0.30 [time constant: 0.4 seconds] and 100 Hz) and archived under the control of Harmonie version 5.4 (Stellate Systems, Montreal) software. All signals were sampled digitally at 256 Hz; EEG leads and A2 were all referenced to A1 during recording and re-referenced offline to A1+A2.

After participants slept undisturbed for 1 sleep cycle, the REMD group was awakened after 5 minutes of REM sleep by a 100ms, 500Hz tone and were prompted to report any mentation that may have occurred prior to being woken up. They then answered a series of directed questions concerning their dream mentation. The target question for the present analyses was: "To what extent was the virtual reality experience incorporated in your dream:

1 = *not at all* to 9 = *very much so*". The dream interview procedure ensured that participants were fully awake for at least 10 minutes even in the absence of dream recall. The CTL groups was treated exactly as the REMD group except they were awakened for dream recall after 20 minutes of REM sleep had elapsed in each sleep cycle. Sleep tracings were scored by an experienced polysomnography technician using standard sleep staging criteria (Rechtschaffen and Kales, 1968), whose ratings were then analyzed by an in-house program that calculated, for each sleep stage, 1) time in stage (number of minutes/night) and 2) percent time in stage (%minutes/total sleep time).

Dream Log

Participants were instructed to complete a dream log every morning for post-VR days 1 to 9 which consisted of questions about their previous night's sleep and dreams. The target question was: *To what extent was the virtual reality experience incorporated in your dream: 1 = not at all to 9 = very much so*.

Episodic Memory Task

The episodic memory task consisted of forced choice questions that evaluated the memory of factual/perceptual, spatial and temporal aspects of 1 of eight target indoor locations visited during the VR task. Questions for each of the 8 locations were the same except for details specific to a location (e.g., character's name). Factual and temporal questions were answered by means of a dropdown menu. Spatial questions were answered by placing an "x" on a map of the room (see Figure 2 for an example); although there were a fixed number of places an "x" could be placed, this task may be considered a "cued-recall" task as opposed to a "recognition" task. For each question, participants specified whether their response was accompanied by autonoetic awareness (i.e., previously defined as able to visualize the corresponding scene with the mind's eye) by use of a drop-down menu; choices were: *I remember* (presence of autonoetic awareness), *I know* (absence of autonoetic awareness), or *I don't know*.

Factual/perceptual memory elements of target items tested consisted of 1) object features including type of object (necklace, hourglass, gloves, shoes, perfume bottle, balancing scales, bow or book) and object color (orange, yellow, green, red, purple, yellow,

white or blue) and 2) character features including age (young or old), accent (American or British), hair length (long or short), hair color (blond, brown, black or red), clothing color (black, white, grey, green, red, blue or brown), clothing type (robe, shirt or pants). Spatial memory elements of target items consisted of the location of 1) the table in the room, 2) the object on the table, and 3) the character in the room.

Factual/perceptual memory elements of incidental items consisted of 1) wall-hung object features including type of object (painting or tapestry) and object theme (depiction of a forest or town), 2) type of furniture other than the table (desk, shelves or dresser), 3) furniture-supported object features other than those on the table (vase, cup or bowl), 4) type of object leaning against the furniture other than the table (shovel or broom), 5) carpet features including shape (square or circular) and color (red, green or blue), and 6) type of fireplace (round or square). Spatial memory elements of incidental items consisted of the locations of 1) the chair near the table 2) the object on the wall, 3) the furniture other than the table, 4) the object leaning on the furniture other than the table, 5) the center of the carpet, and 6) the fireplace. Target and incidental items were not matched for familiarity.

Temporal elements were assessed with the following questions: 1) "who did you see before X" and 2) "who did you see after X", where X represents the current location. These questions were answered by selecting one of 5 characters (four target characters and the introductory character) from a drop down menu. Characters were identified by their name and short revealing description that did not involve any features of the memory task (e.g., "the drunk", "the countess", "the very tall man"). Also available was the option "this was the last person I saw). There were no temporal questions relating to incidental objects. All Temporal questions were scored as 'correct' (score of 1) or 'incorrect' (score of 0).

Participants were randomly assigned questionnaires from two locations (one each from the low and high emotion versions of the VR task) for a practice test. On post-VR day 2, questionnaires from two other locations (one each from the low emotion and high emotion versions) were sent by email; this constituted the main dependent measures for the episodic memory task. Factual/perceptual and temporal index scores were calculated as the total number of correct answers on each set of questions. All factual/perceptual and temporal questions were scored as 'correct' (score of 1) or 'incorrect' (score of 0), for a total possible factual/perceptual performance index of 8 for target items and 6 for incidental items, and a total possible temporal performance index of 4.

Spatial error scores were calculated by measuring the distance, in virtual meters, between each participant's indicated answer and the actual location of the target (scores range from 0 to 20). For objects on or around the table, measurement units were scaled to a ratio of 1:4, and scores range from a spatial error of 0 to 4 for object location on a table and 0 to 12 for around the table. A total spatial error index consisted of the sum of spatial errors derived from all the spatial questions, for a maximum spatial error index score of 44 for target objects and 72 for incidental objects. The measure of autonoetic awareness consisted of the total number of "remember" responses given by each participant, for a maximum of 8 for factual/perceptual target items, 6 for factual/perceptual incidental items, 4 for temporal performance, 3 for spatial target items and 6 for spatial incidental items.

Data was analyzed using 2x2 manovas with condition (REMD, CTL) as a between groups factor and task (low, high emotions) as a repeated measures factor. A first manova utilized factual, spatial and temporal performance scores of target items as dependent measures. A second manova used factual, spatial and temporal autonoetic scores of target items as dependent measures. Subsequent manovas used factual and spatial performance scores (third manova) and autonoetic scores (fourth manova) for incidental items.

For correlations and T-tests, a single score per participant was calculated by averaging the score for the low emotion task from that of the high emotion task.

Results

VR task

The low emotion task took on average 15 minutes and 51 seconds (SD = 3:47; range = 10:24 to 21:32) and the high emotion task took on average 19 minutes and 8 seconds (SD = 6:52; range = 10:59 to 34:29). T-tests revealed that time in task did not differ between groups for the low emotion (p = .96) or high emotion (p =.95) task. Two participants reported mild symptoms of cyber sickness and only completed the low emotion task. The data from these subjects was not used for task comparisons (for a total N of 14), but was used for correlations (total N of 16).

REM sleep *deprivation*

The REMD group had fewer minutes of REM sleep (M = 29.13, SD = 5.44) than the CTL group (M = 56.76, SD = 24.68; $t(12) = 2.89$, $p = .01$) and lower %REM sleep (M = 9.51,

SD = 1.08) than the CTL group (M = 16.71, SD = 5.57; $t(12) = 3.36$, $p = .005$). The REMD group also had higher %Stage 4 sleep (M = 25.57, SD = 6.65) than the CTL group (M = 18.91, SD = 5.11; $t(12) = -2.10$, $p = .058$) and more minutes of Stage 2 sleep in the last third of the night (M = 65.53, SD = 16.95) than the CTL group (M = 49.43, SD = 7.55; $t(12) = 2.29$, $p < .05$). The groups did not significantly differ in terms of total sleep time (p = .5). Details are shown in Table 1.

Task performance

Performance index scores were subjected to a group (REMD vs. CTL) x task (low vs. high emotions) manova for target and incidental items separately; results are presented in Table 2 and Figure 3. A group main effect for memory of factual/perceptual target elements ($F_{1,25} = 5.30$, p = .03) indicated that the REMD group (M = 4.50, SD = 1.65) performed better than the CTL group (M = 3.14, SD = 1.24). This measure correlated positively with %SWS ($r_{16} = .614$, p > .02) and negatively with %REM sleep ($r_{16} = -.637$, p < .01) (see Figure 4).

A second group main effect for memory of spatial incidental elements ($F_{1,25} = 7.82$, p = .01) indicated that the REMD group demonstrated more spatial errors (M =21.64, SD = 6.09) than the CTL group (M =15.36, SD = 4.45). Spatial errors did not correlate with any sleep measures. Nor did they correlate with memory of factual/perceptual target elements.

No main effects were observed for memory of target or incidental temporal elements. Also, no significant main effects were found for memory of low emotion vs. high emotion task elements; there were, however, two interactions involving task reported further in the 'autonoetic awareness' section below.

Autonoetic awareness

A group main effect for autonoetic awareness during recognition of factual/perceptual target elements ($F_{2,25} = 10.04$, p = .004) revealed that the REMD group (M = 4.71, SD = 2.16) reported more "remember" responses than the CTL group (M = 2.07, SD = 1.59). Additionally, two *group* x *task* interactions revealed effects of REM sleep deprivation that were specific to low emotion, but not high emotion, target spatial elements: 1) an interaction for low emotion task spatial errors ($F_{1,25} = 4.09$; p < .05) in which the REMD group had fewer errors (M = 5.57, SD = 3.73) than did the CTL group (M = 9.71, SD = 3.25; $t(12) = 2.21$, $p < .05$; no difference for high emotiona task), and 2) an interaction for autonoetic

awareness during low emotion spatial recall ($F_{2,25} = 4.08$; $p < .05$) in which the REMD group (M =1.43, SD = 1.13) reported more "remember" responses than did the CTL group (M = 0.14, SD = 0.38; $t(12) = -2.84$, $p < .02$; no difference for high emotion task).

Minutes of Stage 2 sleep were correlated positively with "remember" responses for both factual/perceptual (r = .528, p < .05) and spatial (r = .579, p = .03) target elements. More specifically, minutes of Stage 2 sleep in the last third of the night correlated with autonoetic awareness for recognition of factual/perceptual elements (r = .594, p = .015) and with autonoetic awareness for recognition of spatial elements (r = .685, p = .003) whereas minutes of Stage 2 sleep in the first and second thirds of the night did not.

Dreaming

During REM awakenings, 11 participants (68%) reported incorporating the VR task in their dream, although in most instances the incorporation was only weakly related to the task, i.e., the average score was 2.61 (SD = 1.12) on a scale of 1 to 9. These incorporation ratings did not correlate with any measure of the episodic memory task.

Scores from the home dream logs reveal that half of the participants (N = 8) reported incorporating some aspect of the task in the post-VR period. Regardless of REMD vs. CTL grouping, participants were classified as "incorporators" if they scored an average incorporation of >0; otherwise they were classified as "non-incorporators". As shown in Table 3, incorporators and non-incorporators had equal distributions of REMD and CTL participants and did not differ significantly in sleep stage composition. T-tests revealed that incorporators tended to have fewer spatial errors (M = 6.31, SD = 3.28) than did non-incorporators (M = 9.44, SD =3.26; $t(14) = -1.19$, $p = .08$). In contrast, no significant differences or trends were found for measures of factual/perceptual recall (p < .20), temporal recall (p < .30) or autonoetic awareness (p < .40). As illustrated in Figure 5, the spatial error index was negatively correlated with incorporation on post-VR days 1-2-3-4 (r = -.523, p < .03), and (marginally) total incorporation (r = -.421, p < .10), but not with incorporation on days 5-6-7-8 (r = -.275, p < .30), or incorporation in dreams reported after experimental awakenings (r = -.329, p < .30).

Discussion

The present study used a novel VR task in conjunction with a REM sleep deprivation procedure to clarify the role of sleep and dreaming in episodic memory processing. The VR task permitted an ecologically valid measure of episodic memory by engaging participants in life-like events. Importantly, the task allowed a systematic manipulation of variables that are known to modulate encoding and recall/recognition, namely, the emotional salience of item locations and the participant's intention to remember.

Contrary to expectations, the REMD group had better recognition of factual\perceptual components of the episodic memory task than did the CTL group. This finding may relate to the fact that the REMD group also had more SWS than the CTL group, a notion that is supported by a positive correlation between this measure of episodic memory and minutes of SWS. This finding is also consistent with previous studies that have associated SWS with the consolidation of the factual aspects of declarative memory as seen in studies of word list memorization (Fowler, Sullivan and Ekstrand, 1973; Plihal and Born, 1999; Gais, Molle, Helms and Born, 2002; Gais and Born, 2004). SWS may be conductive to the processing of declarative memory (Diekelmann and Born, 2010) as suggested by the finding that an increase in slow wave activity induced by transcranial magnetic stimulation during SWS improves memory on a word pair task (Marshall, Molle, Hallschmid and Born, 2004). The current study suggests further that the beneficial effect of SWS for the consolidation of factual\perceptual aspects of declarative memory applies only to items that are actively encoded (target items). In effect, recognition of factual/perceptual items that participants were not instructed to pay attention to (incidental items) did not differ between groups and was not associated with SWS. However, the higher amount of incidental objects as compared to target objects may have made it more difficult to remember the former, and thus may account for a lack of a significant effect. Nonetheless, the memory of the spatial locations of incidental items was reduced in the REMD group, suggesting that spatial information of actively and passively encoded items is processed in different sleep stages.

Autonoetic Awareness

Autonoetic awareness during the recognition of factual\perceptual and spatial aspects of the VR task was strongly correlated with the amount of late night Stage 2. As such, the finding that the REMD group reported more “remember” responses in relation to

factual/perceptual elements than did the CTL group may relate to the fact that the REMD group had more Stage 2 sleep during the last third of the night. These results are consistent with the previous finding that autonoetic awareness during recognition of the episodic-like "What, When, Where" task is associated with late night as opposed to early night sleep (Rauchs et al., 2004). While the authors attribute this effect to REM sleep due to the predominance of this stage during the second half of the night, their results could also be due to late-night Stage 2 sleep that is present at that time. Our finding of a strong association between autonoetic awareness and Stage 2 in the last third of the night suggests that features specific to late Stage 2, such as increased spindle activity (Jankel and Niedermeyer, 1985; Guazzelli, Feinberg, Aminoff, Fein, Floyd and Maggini, 1986), may underlie the present finding. Indeed, sleep spindles have been associated with declarative learning (Gais et al., 2002; Schabus, Gruber, Parapatics, Sauter, Klosch, Anderer, Klimesch, Saletu and Zeitlhofer, 2004; Schmidt, Peigneux, Muto, Schenkel, Knoblauch, Munch, de Quervain, Wirz-Justice and Cajochen, 2006; Genzel, Dresler, Wehrle, Grozinger and Steiger, 2009); and plasticity (Steriade, 1999). It is noteworthy that other studies examining the role of sleep stages in autonoetic awareness (Drosopoulos, Wagner and Born, 2005; Daurat et al., 2007) have also utilized an early night/late night paradigm and thus may also have overlooked a role for Stage 2. However, in contrast to Rauchs et al. (2004) and the present findings, these studies reported an association of autonoetic awareness with early night sleep. This may indicate that sleep-dependent processing associated with the autonoetic awareness of episodic-like tasks (Rauchs et al., 2004) differs from that implicating autonoetic awareness of word lists (Drosopoulos et al., 2005; Daurat et al., 2007).

Emotions

Contrary to previous findings of an association between emotional memory and REM sleep (Wagner et al., 2001; Nishida et al., 2009), recall/recognition performance on the low emotion and high emotion tasks were similarly affected by REM sleep deprivation. It is possible that both conditions were in fact emotionally arousing and novel due to the participation in an engaging story within a realistic, immersive environment. Indeed, greater differences between low emotion and high emotion conditions, such as those found between the neutral and emotional stories of Wagner et al., (2001) may be necessary to induce a differential need for REM sleep-processing. For example, in the latter study the neutral

stories concerned the manufacture of a bronze sculpture and clothing presented in a fashion show, and thus sharply contrasted with emotional stories that dealt with a child murder and difficulties (including sexual) of a paraplegic. We opted to remove many of the most horrific features available in the Oblivion program because of their disturbing nature. Thus, the failure to replicate a REM sleep association with items from our high emotion task may be the result of insufficient differences in arousal and affect between the low emotion and high emotion conditions. It should be noted that observed lack of significant effects may be due to the low number of subjects in the study, i.e., 14 subjects in two groups.

However, we did observe an interaction between *task* and *group* where the REMD group performed better and reported more "remember" responses for the spatial aspects of the episodic memory task in the low emotion but not high emotion tasks. This result may reflect a specialized role for REM sleep in the processing of emotional memory, whereas the benefit of the SWS increase observed in the REMD condition may have been nullified by the loss of REM sleep in the high emotion task but not the low emotion task.

Dreaming

It has been previously demonstrated that dreaming of a spatial task during a NREM nap is associated with improved performance on that task (Wamsley et al., 2010). In this study, a small number of participants (N = 4; 8%) who incorporated the task into mentation at sleep onset (N = 3) or during Stage 2 sleep (N = 1) exhibited increased learning on a virtual maze task. While we found no link between task incorporations into mentation from experimental REM awakenings and subsequent task performance, we found an association between total task incorporation on post-VR days 1, 2, 3 and 4 and performance on spatial aspects of the task, which occurred on post-VR day 2. This suggests that for the present study task incorporation is not predictive of later performance but rather a consequence of performance. In addition, our results are in line with those of Wamsley et al. (2010) in that dreaming about an episodic task is associated with improved memory for spatial aspects of this task, and not its temporal or factual/perceptual aspects.

Increased SWS in the REMD group

We observed that the REMD group received more stage 4 than the CTL group. This serendipitous finding of increased SWS in face of REM deprivation may be of relevance to the current debate concerning the relationship, or lack thereof, between REM and NREM homeostatic processes. The relationship between regulatory processes of REM sleep and SWS are not well understood, with some studies suggesting that homeostatic regulatory processes of REM sleep are independent of those regulating NREM sleep (Vivaldi et al., 1994; Ocampo-Garces et al., 2000; Franken, 2002), while others suggest that the amount and frequency of REM sleep is regulated by the homeostatic regulation of NREM sleep (Benington and Heller, 1994). Shea et al., (2008) report an increased total percentage of NREM sleep in rats during selective REM sleep deprivation, a finding that closely parallels our observations. Our results similarly support the notion that REM sleep and SWS homeostatic processes are not independent.

Summary and conclusion

Episodic memory is a complex, multi-faceted cognitive process that engages a wide neural network spanning prefrontal, parietal and temporal lobes (Hassabis, Kumaran and Maguire, 2007; Addis, Pan, Vu, Laiser and Schacter, 2009). Each of its components, i.e., its factual/perceptual, temporal, spatial and autonoetic features, can be viewed as separate processes that require proper coordination such that memory traces become events that may be reviewed with the "mind's eye". With growing evidence that different components of sleep are associated with these different memory processes, it is not surprising that the elements of episodic memory identified in the present study are differentially associated with REM and NREM sleep attributes. The present results confirm a relationship between factual declarative memory and SWS, and add that this relationship may hold true only for items that are actively, but not passively, encoded. The results also confirm a previously reported association between late night sleep and autonoetic awareness during recognition, and adds that this relationship may be mediated by late night Stage 2 and not REM sleep as previously suggested. Finally, the results confirm the finding that incorporating a task into one's dreams is associated with better performance on the spatial features of an episodic memory task but not on its factual/perceptual or temporal features. Together, the results suggest that episodic memory benefits from the coordination of several sleep-related processes acting differentially upon different memory components.

Table1. Sleep stage differences between groups.

	CTL		REMD			
	Mean	***SD***	**Mean**	***SD***	**t**	
Min S1	38.16	*(21.72)*	22.34	*(12.84)*	1.66	
% S1	12.70	*(9.65)*	7.30	*(3.82)*	1.38	
Min S2	141.41	*(32.81)*	142.23	*(29.78)*	-0.05	
1st 1/3	41.96	*(17.48)*	33.37	*(13.75)*	1.02	
2nd 1/3	42.36	*(11.27)*	51.06	*(10.87)*	-1.47	
3rd 1/3	**49.43**	*(7.55)*	**65.53**	*(16.95)*	**-2.29**	*
% S2	42.60	*(5.35)*	46.64	*(8.55)*	-1.06	
1st 1/3	13.34	*(4.98)*	10.31	*(4.34)*	1.21	
2nd 1/3	13.69	*(2.08)*	15.80	*(4.08)*	-1.22	
3rd 1/3	16.20	*(1.85)*	19.79	*(4.25)*	-2.05	†
Min S3	30.29	*(19.77)*	36.39	*(29.17)*	-0.46	
% S3	9.10	*(5.71)*	10.96	*(6.82)*	-0.55	
Min S4	62.91	*(22.27)*	78.37	*(24.29)*	-1.24	
% S4	**18.91**	*(5.11)*	**25.57**	*(6.66)*	**-2.10**	‡
Min REM	**56.76**	*(24.69)*	**29.13**	*(5.44)*	**2.90**	**
% REM	**16.71**	*(5.57)*	**9.51**	*(1.08)*	**3.36**	**
Min Total sleep	329.53	*(53.15)*	308.46	*(60.81)*	0.69	

‡ $p = .06$

* $p < .05$

** $p < .01$

Table 2. Results of the ANOVAs performed.

Memory Performance Index –Target Items

	Main Effect of REM sleep deprivation	Main Effect of Emotions	Interaction effect
Factual	**F = 4.52 ; P = .03**	F = 0.36 ; P = .55	F = 0.45 ; P = .51
Spatial	F = 2.22 ; P = .15	F = 0.28 ; P = .60	**F = 4.09 ; P < .05**
Temporal	F = 0.96 ; P = .34	F = 0.20 ; P = .66	F = 1.34 ; P = .26

Memory Performance Index –Incidental Items

	Main Effect of REM sleep deprivation	Main Effect of Emotions	Interaction effect
Factual	F = 0.07 ; P = .80	F = 0.13 ; P = .71	F = 0.33 ; P = .57
Spatial	**F = 5.49 ; P = .03**	F = 1.87 ; P = .18	F = 0.11 ; P = .75

Remember Responses –Target Items

	Main Effect of REM sleep deprivation	Main Effect of Emotions	Interaction effect
Factual	**F = 10.04 ; P = .004**	F = 0.003; P = .96	F = 0.45 ; P = .51
Spatial	F = 1.11 ; P = .31	F = 0.79 ; P = .38	**F = 4.08 ; P < .05**
Temporal	F = 0.03 ; P = .84	F = 0.04 ; P = .85	F = 0.35 ; P = .56

Remember Responses – Incidental Items

	Main Effect of REM sleep deprivation	Main Effect of Emotions	Interaction effect
Factual	F = 0.92 ; P = .35	F = 0.23 ; P = .63	F = 0.23 ; P = .63
Spatial	F = 0.38 ; P = .54	F = 0.42 ; P = .84	F = 0.04 ; P = .84

Table 3. Comparisons between the incorporator and non-incorporator groups.

	Incorporators	Non-incorporators
Group	4 REMD, 4 CTL	4 REMD, 4 CTL
Sex	1 Male, 7 Females	2 Males, 6 Females
% S1	12.02 (±9.41)	8.06 (±3.16)
% S2	43.95 (±8.55)	46.50 (±5.07)
% S3	11.22 (±6.79)	9.29 (±4.75)
% S4	20.96 (±5.70)	20.99 (±8.71)
% REM	11.81 (±2.49)	15.20 (±7.01)

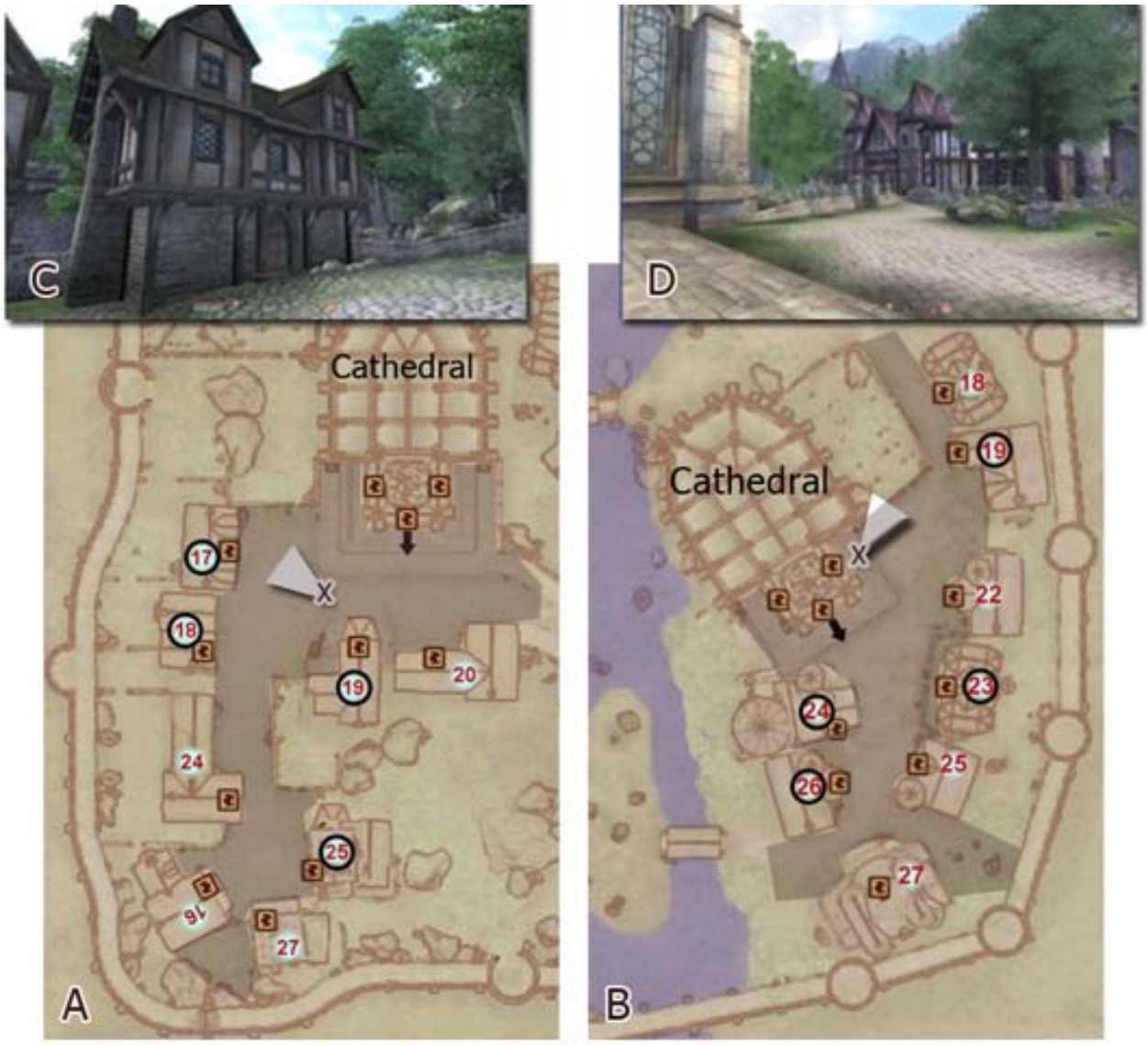
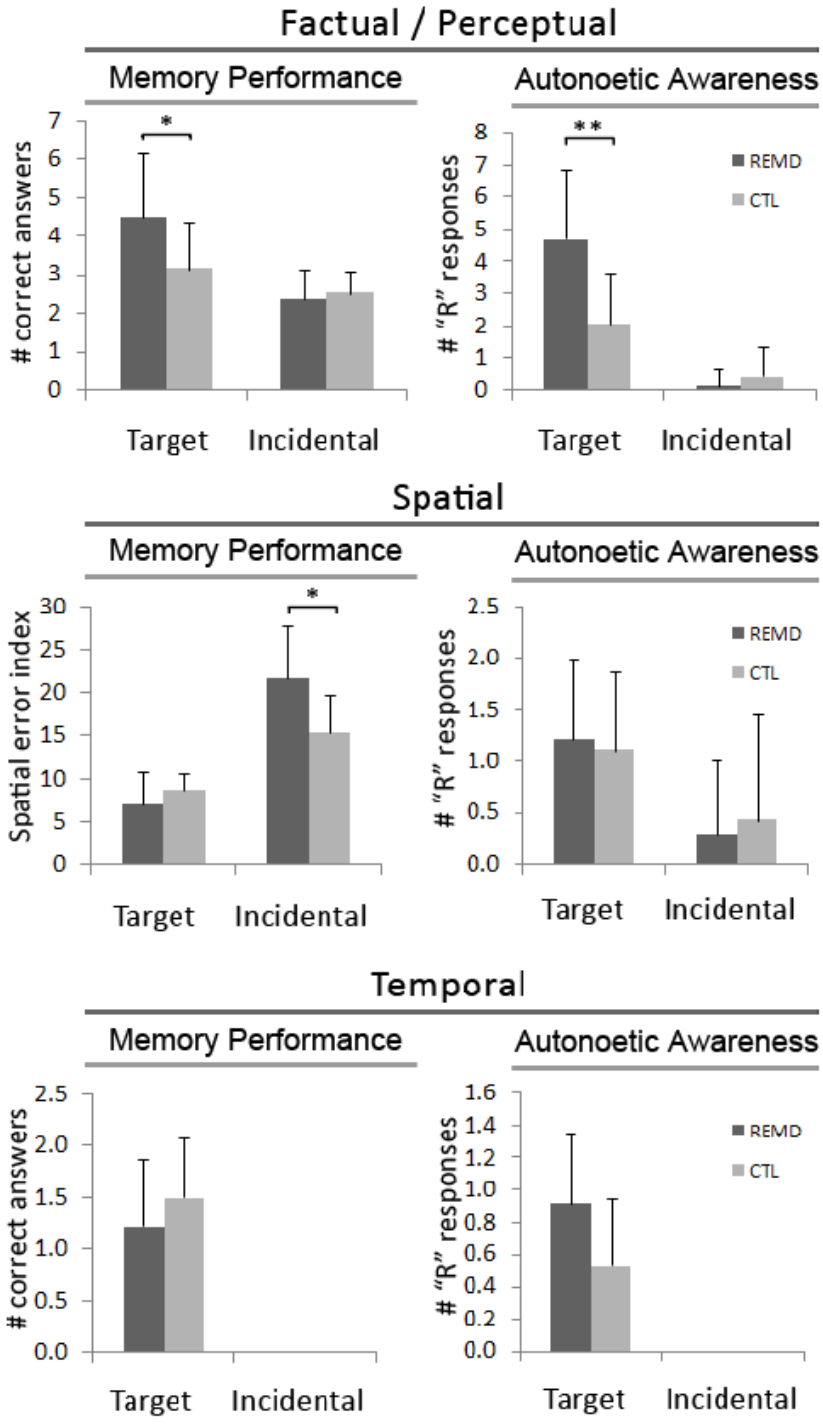


Figure 1. Spatial layout of the two towns. The town of the low emotion task (A) and of the high emotion task (B) were similar in number and positioning of houses (identified by a number), target houses (circled numbers) and total navigational area (shaded area between houses). The arrows identify the task starting point. The "Xs" identify the location from which the in-task perspectives "C" and "D" were taken, whereas the triangle indicates the angle of the perspective. "C" was taken from the middle of the town square and looks towards building A-17. "D" was taken from the steps of the cathedral and looks outward to building B-18. Also visible are the fences that keep players within the navigational area.

Figure 2. Example of the interior of a house, its items, and related recall task materials. A) In-task perspective of what participants see when entering target house 18 of the low emotion task. To the right is the table containing the target object, and center left is the character. Also present are incidental items (desk, vase, shovel, painting, fireplace, carpet and chair). B) Close up view of the character. C) Recall questionnaire item concerning the spatial location of the target object on the table. The participant placed an "X" where she believed the object was placed and the difference in ¼ meters from the actual object location consists of the spatial error score for this item. Participants mouse-clicked the figure to place an "X", and clicked again to remove it for adjustments. D) Close up view of the object (yellow balancing scale) on the table. All tables had candles in their centers to highlight the fact that

the table contains the target object. E) Layout of the room for recall questionnaire items situated in the room. Participants placed an “X” on a similar figure for all questions relating to spatial locations within the room. Each question had its own copy of the figure, and each room had a specific figure. Every room had a unique layout that was matched for size.



**p = .004

*p = .03

Figure 3. Performance and "remember" ("R") responses on the factual/perceptual, spatial, and temporal aspects of the recall task as a function of REM sleep deprivation. Temporal questions did not have an incidental component.

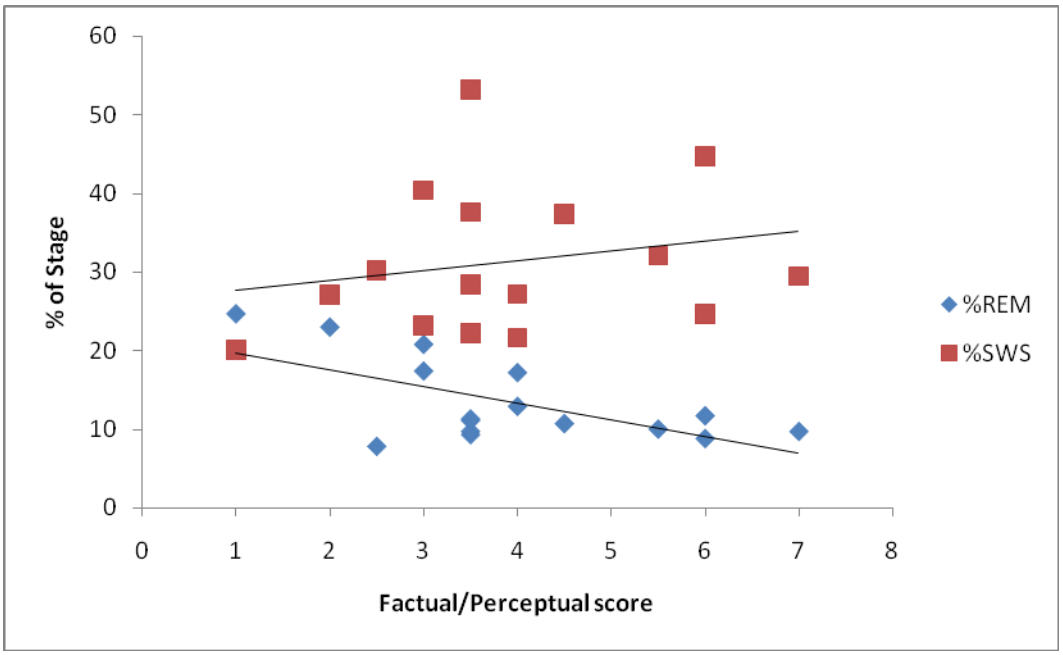


Figure 4. Factual/perceptual scores as a function of % of REM sleep and SWS. Regression lines for the two groups reflect opposite effects, i.e., a positive correlation with %SWS (r_{16} = .614, $p > .02$) and a negative correlation with %REM sleep (r_{16} = -.637, $p < .01$).

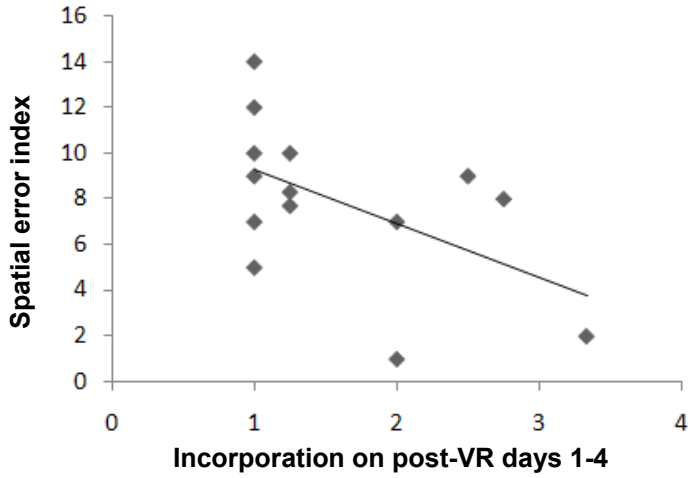


Figure 5. Relationships between the amount of incorporation of the task into dream content on post-VR days 1-4 and recall of the spatial locations of target items. The spatial error index was positively correlated with incorporation on post-VR days 1-2-3-4 ($r_{16} = -.523$, $p < .03$).

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Spatial memory performance shifts its association from SWS to REM if task is emotional

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Abstract

While a substantial body of evidence links slow wave sleep (SWS) to the processing of declarative memory, a small but growing number of studies indicate a role for rapid eye movement (REM) sleep in the processing of declarative memories with an emotional tone. One possible explanation for these results is that tasks administered for sleep-related emotional declarative learning are different from those used in studies investigating sleep-related neutral declarative learning. Another, more intriguing possibility is that imbuing a declarative task with emotional qualities shifts its dependence from SWS to REM sleep. Here we examine if spatial memory, previously shown to be strongly associated with SWS, shifts to a REM sleep association if emotional elements are associated with the task. Participants navigated two virtual towns, one high emotion (high emotion or dysphoric task) and one low emotion (low emotion task). Half of participants were subjected to a REM deprivation procedure during post-task sleep (REMD group) while others underwent control awakenings after 25 minutes of REM (CTL group). Memory of the location of visited areas was tested 10 to 12 days later. The REMD group performed less well than the CTL group on the emotional task, the performance on which correlated with the amount REM sleep. In contrast, the REMD group performed better than the CTL group on the neutral task, the performance on which correlated with Stage 4 sleep. This demonstrates, for the first time, that the presence of emotions during a task may modulate the sleep stage with which its consolidation is associated.

Introduction

It is now well established that sleep is involved in the processing of memory (Walker & Stickgold, 2006). The mammalian brain cycles through two dramatically different states throughout the night and studies are revealing how the unique properties of these states contribute to specific facets of memory. In particular, cortical slow wave and hippocampal ripple activity characterizing SWS sleep are believed to support the reactivation of declarative memory traces and to facilitate their integration within neocortical areas (Diekelmann & Born, 2010). This possibility is supported by studies finding an association between SWS and the learning of word lists (Fowler, Sullivan & Ekstrand, 1973; Plihal & Born, 1999; Gais, Molle, Helms & Born, 2002; Gais & Born, 2004) and performance on spatial tasks (Plihal & Born, 1999; Peigneux, Laureys, Fuchs, Collette, Perrin, Reggers, Phillips, Degueldre, Del Fiore, Aerts, Luxen & Maquet, 2004; Rasch, Buchel, Gais & Born, 2007; Rudoy, Voss, Westerberg & Paller, 2009). These studies are consistent with the 'dual-process hypothesis', which posits that SWS is involved with hippocampus-dependent, declarative memory while REM sleep is implicated in hippocampus-independent memory that is not of a declarative nature.

Notable exceptions to the dual-process hypothesis are found in three studies in which declarative tasks containing material of an emotional nature were found to depend upon REM sleep. The unique neurophysiology of REM sleep, namely the increased activity in cortical theta, elevated acetylcholine levels and increased amygdala activity, may implicate this stage of sleep in emotional memory processing (Walker, 2009; Walker & van der Helm, 2009). An early finding that REM deprivation reduced recall of emotional, but not neutral stories (Greenberg, Pearlman, Schwartz & Grossman, 1983) was confirmed and extended by Wagner et al. (2001) who reported that emotional, but not neutral stories are better remembered after sleeping for the REM-rich second half of the night as compared to the SWS-rich first half of the night. A more direct role of REM sleep in the processing of emotional stimuli was suggested by the finding that memory of emotional, but not neutral pictures, was associated with the amount of REM sleep during a nap and, in addition, to the amount of theta activity contained within the REM period (Nishida, Pearsall, Buckner & Walker, 2009). These studies are notable because they suggest that emotional and neutral declarative memories may be differentially consolidated during sleep and that REM sleep may play a specialized role in the

processing of emotional memory.

However, the relationship between REM and emotional stimuli may be task specific because studies that have examined emotional declarative memory used stimuli (pictures and stories) that differed in type from those used in studies of non-emotional declarative memory (word pairs & spatial learning). In fact, the neutral versions of the emotional tasks (neutral pictures and neutral stories) do not seem to be dependent upon SWS (Wagner et al., 2001; Nishida et al., 2009), suggesting that sleep-related processing of these tasks may differ in key respects from neutral tasks that have been found to be SWS-dependent (word lists and spatial learning). A strong demonstration of the specialized role of REM sleep in the processing of emotional declarative memory would require that a given SWS-dependent task shift its dependence to REM sleep when this task is emotional in nature. The current study directly tested this possibility by having participants undergo two matched spatial navigation tasks that differed only in emotional load and observing how performance in each task was affected by selective REM deprivation.

A spatial task was selected for this study because its association with SWS sleep had been well established by previous studies (see above). Its association with REM sleep has been demonstrated only for rodents; learning in the water maze task is paralleled by increases in REM sleep (Smith & Rose, 1997) and is disrupted by REM deprivation (Smith & Rose, 1996; Beaulieu & Godbout, 2000; Le Marec, Beaulieu & Godbout, 2001; Yang, Hu, Wang, Zhang, Luo & Chen, 2008; Li, Tian, Ding, Jin, Yan & Shen, 2009). . However, the water maze may be considered an emotional spatial task because the rodent must find a hidden platform to avoid drowning. Spatial tasks used in human research are not generally emotional. Thus, by increasing the emotional load of a spatial task we may determine if its dependence on with SWS will shift towards a dependence on REM sleep. To do this we used a virtual reality technology to create spatial locations that differ in emotional load and examined if REM deprivation affected the spatial memory of the high emotion locations but not the low emotion locations as expected. We further predicted that the amount of post-task REM sleep would positively correlate with recall performance of the high emotion locations while the amount of post-task SWS would positively correlate with recall performance on the low emotion locations.

Methods

Participants

Sixteen healthy volunteers (3 male) aged 18-36 years (mean = 25.1; SD = 5.71) provided written consent to participate in the study, which was approved by the ethic committee of Hôpital du Sacré-Cœur de Montréal. Participants reported no psychiatric, medical, or sleep disturbances. Two participants felt discomfort during the VR task and only completed the low emotion task; these participants were excluded from group comparisons, i.e., manovas and T-tests (N = 14) but included in correlational analyses (N = 16).

Procedures

Participants completed two VR tasks, separated by a 10-min break. Then they were randomly assigned to either a REM sleep deprived (REMD) or a control (CTL) group and slept one night in a sleep laboratory where they underwent experimental awakenings either 5 (REMD) or 25 (CTL) minutes into each REM sleep period beginning after the first. Ten to 12 days post-task participants returned to the laboratory to complete a spatial recall task. They were then debriefed and compensated 75$ for their time. As part of an unrelated study, participants filled out questionnaires at home two, six and nine days post-task concerning episodic details of the task and completed dream logs for 10 days. Results for these measures are not reported here.

Virtual Reality (VR) Task

The VR task was designed with the TES Construction Kit (Bethesda Softworks) and run using the Elder Scrolls VI: Oblivion engine (Bethesda Softworks) on a HP XW4600 computer (Dual Core E6850, 3.00GHz, 4 GB RAM, NVIDIA GeForce 8800GTX video card). The VR interface consisted of an eMAGIN Z800 3DVisor head mounted display in 1024x768 resolution and a wireless mouse. Surround sound was provided by a Sony Home theater 6.1 channel system. The VR task was navigated from a first person perspective.

Participants underwent both the low emotion and high emotion version of the VR task in a counterbalanced order. Each VR task featured a city to be navigated in order to locate and enter target houses where target characters were encountered and target objects obtained (see Figure 1 for the spatial layout of the two cities). The two versions of the task were matched in

their spatial aspects but differed in the emotionality of events and stimuli contained within the houses. In each version of the task, participants were instructed to find and talk to a host character who was located in a small enclosure at the edge of the city. The host situated the participants within the context of the ongoing story and explained to them who they should go see next. For each version of the task, participants searched for and visited 4 single-room houses in an order dictated by the story. A compass at the bottom of the VR screen directed participants towards their target location at all times so wayfinding was not an obstacle to task completion. In each target house, participants listened to dialogue from a target character (thus advancing the story) and retrieved a target item. Houses not involved in the task were locked and could not be entered. Characters, events, and some indoor features of the houses of the high emotion version of the task were emotionally negative in quality, while those in the houses of the low emotion version were specially designed to be low in emotions (see Table1 for details). In addition, the storyline of the high emotion version was more emotionally dysphoric than that of the low emotion version in that elements within the houses and referred to in the storyline were dysphoric. However, the city and houses themselves were not dysphoric in nature.

REM deprivation procedures

Subjects slept in a quiet, electrically shielded, room containing a single bed. A video camera, microphone, and intercom system were used to maintain visual and voice contact at all times. Subjects were recorded with an electrode montage of 19 standard 10-20 electroencephalogram channels, 4 electrooculogram channels (left/right, vertical/horizontal), and 1 electromyogram channel (submental). All-night recordings were made using a Grass Model 12 Neurodata Acquisition System (-6 dB filters with cutoffs at 0.30 [time constant 0.4 seconds] and 100 Hz) and archived under the control of Harmonie version 5.4 software. All signals were sampled at 256 Hz; electroencephalogram signals were referenced to A1 and re-referenced offline to A1+A2.

Post-VR REM sleep was reduced in REMD by waking them after 5 mins of REM sleep beginning with REM period #2. In the CTL group, awakenings were conducted after 20 minutes of REM sleep had elapsed. Awakenings were framed as a “dream collection” procedure, which we have found generates less stress and often even enthusiasm in participants even as they are being REM-deprived. In addition, the duration (at least 10

minutes) and interactive nature of the mentation collection interview, even in the absence of any mentation recall, ensured that participants were fully awake and did not fall back to sleep. Sleep tracings were scored by an experienced polysomnography technician using the standard sleep staging criteria (Rechtschaffen & Kales, 1968) and were then analyzed by an in-house program that calculated, for each sleep stage, 1) time in stage (number of minutes/night) and 2) time in stage (percentage of minutes/total sleep time).

Memory Recall Procedures

Participants were given maps of the two versions of the spatial task (see figure 1), in counterbalanced order, and were instructed to mark the houses they had visited. Memory performance errors were assessed by counting the number of target houses the participant failed to identify, i.e., houses that the participant visited but that were not selected in the memory task (missed targets) and the number of non-target houses incorrectly identified as target houses, i.e., houses that the participant did not visit but that was selected during the memory task (wrong targets).

Statistical analyses

Data was analyzed using 2x2 manovas with condition (REMD, CTL) as a between groups factor and task (low, high emotions) as a repeated measures factor with missed targets and wrong targets as dependent measures. All other tests were T-tests, except when mentioned otherwise.

Results

REM deprivation measures

As shown in Table 2, the REMD group had fewer minutes of REM sleep (M = 29.13, SD = 5.44) than the CTL group (M = 56.76, SD = 24.68; $t(12) = 2.89$, $p = .01$) and lower %REM sleep (M = 9.51, SD = 1.08) than the CTL group (M = 16.71, SD = 5.57; $t(12) = 3.36$, $p = .005$). The REMD group also had more %Stage 4 sleep (M = 25.57, SD = 6.65) than the CTL group (M = 18.91, SD = 5.11; $t(12) = -2.10$, $p = .058$), a finding also reflected in a

higher SWS/REM ratio for the REMD group (M = 3.89, SD = 1.09 vs. M = 1.87, SD = .87; $t(12) = -4.19$, $p = .002$).

Spatial Task Performance

A manova found no interaction effects between task (low emotion, high emotion) and group (CTL, REMD) for missed targets (F = 3.06; p = .93) and wrong targets (F = 3.68; p = .68). Nonetheless, a T-test reveiled that the REMD group had more missed targets than the CTL group on the high emotion version of the task (REMD: M = 2.86, SD = .38; CTL: M = 2.00, SD = .58; $t(12) = -3.29$, $p = .01$). T-test also revealed that the CTL group had more wrong targets than the REM group on the low emotion version (CTL: M = 2.67, SD = .79; REMD: M = 1.43, SD = .787: $t(12) = 2.76$, $p = .02$). No group differences were found for wrong targets in the high emotion version and missed targets in the low emotion version (Figure 2).

Missed targets in the high emotion version of the task were negatively correlated with *minutes in REM sleep* ($r(16) = -0.706$, $p = .005$), and *%REM sleep* ($r(16) = -0.714$, $p = .004$). Wrong targets in the low emotion version of the task were negatively correlated with *min in Stage 4 sleep* ($r(16) = -0.62$, $p = .01$) and *%Stage 4 sleep* ($r(16) = -0.65$, $p = .006$) and positively correlated with *%REM sleep* ($r(16) = 0.55$, $p = .03$).

Discussion

The current findings bridges findings showing, on the one hand, that SWS is associated with declarative memory and, on the other, that emotional declarative memory is associated with REM sleep. The REMD group in the present study received less REM sleep and performed more poorly than the CTL group on spatial recall of an emotionally dysphoric navigation task. In contrast, the CTL group received less SWS and performed more poorly on spatial recall of a matched low emotion navigation task. The notion that REM sleep and SWS played distinct roles in consolidation of the high emotion and low emotion versions of the task, respectively, is further reinforced by the finding that the amount of REM sleep was positively correlated with performance on the emotional version of the task while the amount of Stage 4 sleep was positively correlated with performance on the neutral version. Together, these findings suggest that a declarative spatial memory task will be processed by SWS

processes if it contains no dysphoric components whereas it will be processed by REM processes if the task is imbued with dysphoric stimuli.

The present findings thus provide an explanation for the long-standing issue of why spatial memory is associated with SWS in humans and REM sleep is rodents: spatial tasks administered to rodents are typically emotional (see Smith, 1995) while those applied in human research are not. In light of the current results, this important difference is interpreted as a methodological issue relating to the presence of emotional features at time of encoding as opposed to any major neurobehavioral differences between humans and rodents. This interpretation is consistent with accumulating evidence of functional similarities between human and rodent hippocampi, particularly as the latter are implicated in spatial learning (Kesner & Hopkins, 2006). The interpretation of the results are, however, limited by 1) the small number of subjects and 2) memory measurements comprising of a maximum score of 5 which may have artificially inflated differences. In addition, the intervening memory tasks questionnaires (not reported here) on post-task days two, six and nine may have influenced the current results (e.g., prompted rehearsal), although these questionnaires concerned episodic details of items within houses, while the current results concern the locations of target houses within the town.

Why was REM sleep specifically associated with 'wrong targets' but not 'missed targets' for the dysphoric task? Perhaps a bias towards generating 'false alarms' (mislabeling an unexplored location as containing threatening stimuli, i.e., wrong target), as opposed to 'misses' (mislabeling a threatening location as unexplored, i.e., missed target) is adaptive when an individual is placed in an environment that contains threats. REM sleep's association with emotional memory may promote such a bias. It is less clear, however, why REM sleep was associated with an increased number of wrong targets in the low emotion task. Indeed, it is difficult to explain how an *increase* in a stage of sleep can be associated with *reduced* performance. One possibility is that this finding is an artifact of a SWS effect, as SWS is positively associated with this task measurement and also in a seemingly reciprocal relationship with REM sleep.

The differential association of high emotion and low emotion memories with REM and SWS may relate to unique features of these sleep stages that correspond to known mnemonic processes. Performance on a spatial task in humans is associated with hippocampal reactivation during SWS (Peigneux et al., 2004); similarly, in rodents

hippocampal reactivation of pre-sleep exploratory behavior is observed at the cellular level during SWS (Wilson & McNaughton, 1994; Lee & Wilson, 2002; Ji & Wilson, 2007). This hippocampal reactivation occurs in conjunction with sharp wave ripples (Wilson & McNaughton, 1994; Molle, Yeshenko, Marshall, Sara & Born, 2006; Peyrache, Khamassi, Benchenane, Wiener & Battaglia, 2009) which have been associated with learning (Ego-Stengel & Wilson, 2009; Girardeau, Benchenane, Wiener, Buzsaki & Zugaro, 2009; Ramadan, Eschenko & Sara, 2009) and which may promote synaptic potentiation (Bramham & Srebro, 1989). Hippocampal reactivation is also paralleled by replay in neocortical areas such as the prefrontal (Peyrache et al., 2009), parietal (Qin, McNaughton, Skaggs & Barnes, 1997) and visual cortex (Ji & Wilson, 2007). Together these findings suggest that that SWS sleep is ideally suited for processing declarative memories and integrating them within neocortical areas (Diekelmann & Born, 2010).

Hippocampal reactivation of pre-sleep exploratory behavior has also been found in REM sleep (Louie & Wilson, 2001). However, at this time the hippocampus and the amygdala are co-activated and synchronized in the theta frequency band. The latter is a characteristic of REM sleep thought to underlie its implication in emotional declarative memory processing (Pare & Gaudreau, 1996; Hegde, Singh, Chaplot, Shankaranarayana Rao, Chattarji, Kutty & Laxmi, 2008; Karashima, Katayama & Nakao, 2010). This is suggested by the fact that emotional memory formation in the waking state involves the co-activation (Hamann, Ely, Grafton & Kilts, 1999; Canli, Zhao, Brewer, Gabrieli & Cahill, 2000; Dolcos, LaBar & Cabeza, 2004) and theta-band synchronization (Seidenbecher, Laxmi, Stork & Pape, 2003; Pape, Narayanan, Smid, Stork & Seidenbecher, 2005) of the hippocampus and the amygdala. Theta band activity is involved in synaptic plasticity in the hippocampus (Larson & Lynch, 1986; Staubli & Lynch, 1987) and in amygdala (Heinbockel & Pape, 2000; Pollandt, Drephal & Albrecht, 2003)In REM sleep, hippocampal/amygdalar theta synchronization is enhanced in association with increased P wave density (Karashima et al., 2010). P waves, too, are associated with increased plasticity–related gene expression in the hippocampus and amygdala (Datta, Li & Auerbach, 2008). Thus, REM sleep is very likely neurobiologically suited to modulate networks critically involved in emotional memory.

The current findings are consistent with the notion that the unique neurophysiological profiles of REM and SWS may differentially benefit different facets of declarative memories. While both stages are associated with hippocampal reactivation and plasticity, the

hippocampal-neocortical interplay found in SWS and driven by sharp wave ripples suggests a role for declarative memories in general, while the hippocampal-amygdalar interplay found in REM sleep and driven by theta band activity suggests a role in emotional declarative memory in particular. Consequently, all declarative memories may benefit from SWS insofar as they are hippocampal-dependent, while emotional memories may require less SWS-processing because of the additional processing they receive in REM sleep. The possibility that emotional declarative memories are processed in REM sleep at the expense of SWS processing would thus account for the present finding that imbuing a spatial memory task with dysphoric emotions switches its association from SWS to REM sleep. Sleep stages may interact to effect optimal processing of declarative memories depending upon emotional contingencies.

Table 1. Select stimuli from the low-emotion and dysphoric versions of the spatial task

	Low emotion Task	Dysphoric Task
City	Neutral 	Neutral 
Houses	Neutral 	Neutral 
Story	Mild but entertaining A "who-did-it" mystery concerning a stolen painting.	Emotional A series of confiscations, murders and arrests resulting from a corrupt official's greed.
Characters in houses	Low emotion & Friendly 	Angry 
Dialogue	Low emotion What the characters were doing during a particular night (star gazing; working); how the Count was a good leader.	High emotion How the corrupt official's actions are affecting the Character and the city; how to bring him to justice.
♫	Low emotion Soft orchestral music in major key	High emotion Sinister music in minor key
Events	Low emotion - Sheep walking around. Character N1 moves away from door. - Character N2 reading book. - Character N3 faces away from front entrance. - Character N4 faces away from the door, bottles are on the ground.	High emotion -Character E1 gets attacked by and kills a mountain lion hidden in the room. -Character E2 argues with a city guard who is in his house. The character draws a blade and is promptly killed. -Character E3 is led into a trap by another character and is murdered. -When participant picks up target item Character E4 cries thief. A city guard enters the house and arrests and attacks the participant.

Table 2. Sleep stage differences between groups.

	CTL		REMD			
	Mean	***SD***	**Mean**	***SD***	**t**	
Min S1	38.16	*(21.72)*	22.34	*(12.84)*	1.66	
% S1	12.70	*(9.65)*	7.30	*(3.82)*	1.38	
Min S2	141.41	*(32.81)*	142.23	*(29.78)*	-0.05	
% S2	42.60	*(5.35)*	46.64	*(8.55)*	-1.06	
Min S3	30.29	*(19.77)*	36.39	*(29.17)*	-0.46	
% S3	9.10	*(5.71)*	10.96	*(6.82)*	-0.55	
Min S4	62.91	*(22.27)*	78.37	*(24.29)*	-1.24	
% S4	**18.91**	*(5.11)*	**25.57**	*(6.66)*	**-2.10**	‡
Min REM	**56.76**	*(24.69)*	**29.13**	*(5.44)*	**2.90**	*
% REM	**16.71**	*(5.57)*	**9.51**	*(1.08)*	**3.36**	*
Min Total sleep	329.53	*(53.15)*	308.46	*(60.81)*	0.69	

‡ $p = .06$

* $p < .01$

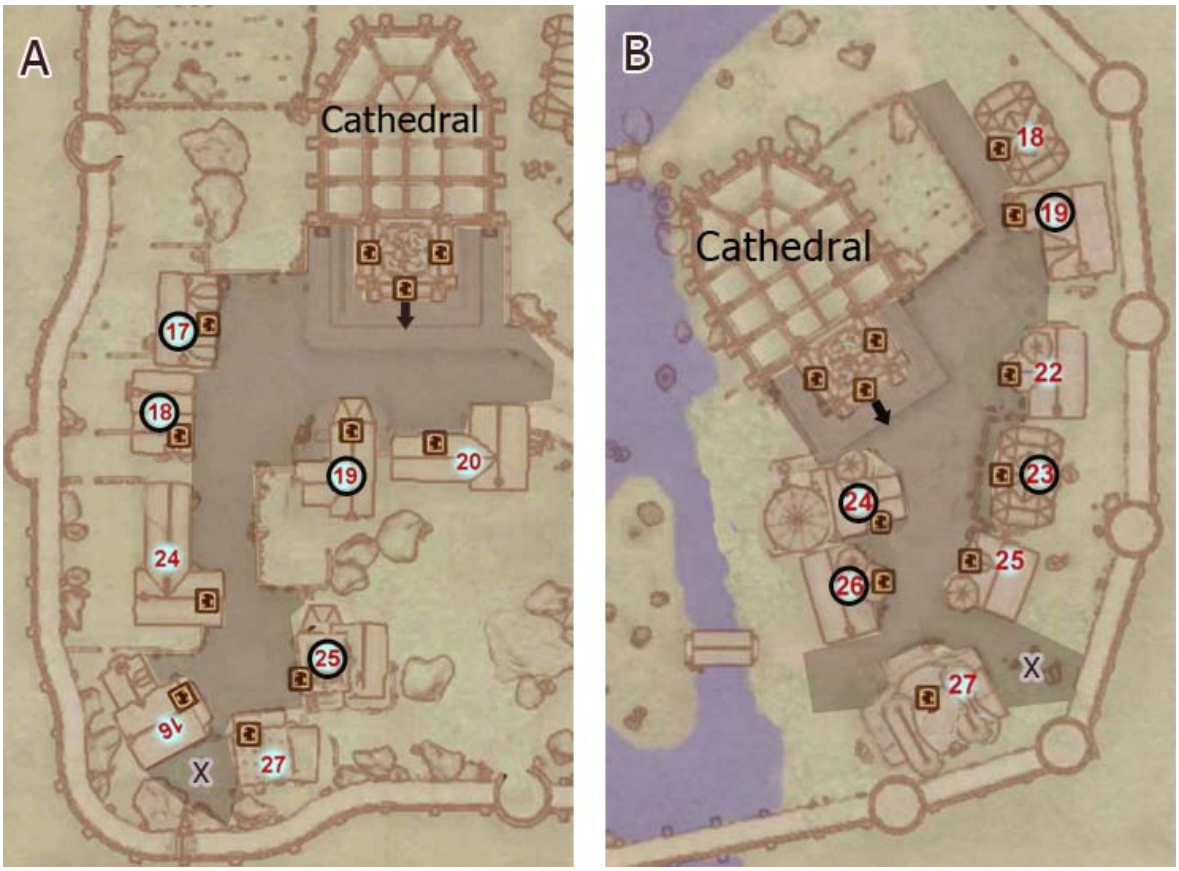

Figure 1. Low emotion and dysphoric versions of the spatial memory task. Spatial layout of the city in the neutral task (A) is comparable in size, layout and appearance to that of the city in the emotional task (B). Navigation was limited to the shaded area by means of walls and fences. An "X" marks the locations of the host characters. Numbers indicate houses; circled numbers indicate target houses. Black and yellow icons indicate doors leading into houses. Arrows indicate the starting point of the task (the cathedral's front door). To test recall, cities were printed on separate page with markings identifying target areas and shaded navigation zones removed. Participants were required to indicate the locations of target houses.

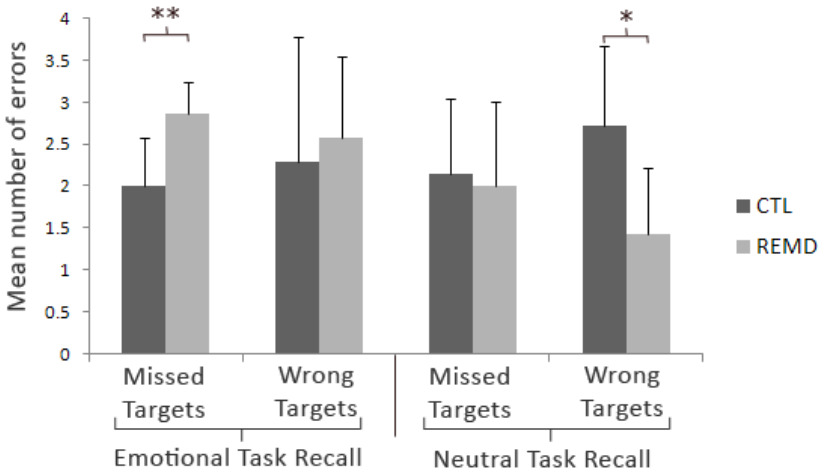

Figure 2. Number of recall errors for the dysphoric and low emotion tasks as a function of the effect of REM deprivation depends on the task. REM deprivation produced more missed targets for the emotional task but fewer wrong targets for the neutral task.

**p = .01

*p = .02

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CHAPTER III

Mentation during sleep onset theta bursts in a trained subject: A role for NREM stage 1 sleep in memory processing?

Article III- Mentation during sleep onset theta bursts in a trained subject: A role for NREM stage 1 sleep in memory processing?

Author Contributions

PS and TN conceived and designed the experiments, PS and ES performed the experiment, PS analyzed the data, and PS and TN wrote the paper.

Mentation during sleep onset theta bursts in a trained subject: A role for NREM stage 1 sleep in memory processing?

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Abstract

NREM stage 1 sleep, known as a brief interval of transition from wake to sleep, is characterized by neurophysiological events and subjective sensory experiences that suggest the stage may be involved in memory processing. To examine this possibility, we conducted multiple awakenings with a trained participant during short bursts of theta activity defining the 5th sub stage of NREM stage 1 sleep (NREM1Φ). Awakenings provided frequent reports of vivid dreaming containing coherent scenes—as opposed to isolated objects often associated with general sleep onset imagery. Analyses of the temporal and semantic aspects of the memories associated with this imagery suggest that multiple memories are selected for incorporation in NREM1Φ imagery on the basis of their semantic proximity and temporal remoteness. Analyses also demonstrate a remarkable pattern in about a third of dreams in which distinct, semantically related memories dating from as little as 10 minutes to as much as 15 years ago were bound in close temporal and spatial proximity within the novel contexts of the imagery. This offline manipulation of semantic information, observed here at a phenomenological level, bears a resemblance to processes thought to underlie *integrative encoding*, i.e., the encoding of an association between events that were not experienced together but which are subsequently combined because they contain at least one overlapping element. This preliminary study provides evidence consistent with the notion that hippocampal-mediated memory processing occurs during the theta bursts found at sleep onset.

"I turned the chair to face the fireplace and slipped into a languorous state. Again atoms fluttered before my eyes. Smaller groups stayed mostly in the background this time. My mind's eye, sharpened by repeated visions of this sort, now distinguished larger figures in manifold shapes. Long rows, frequently linked more densely; everything in motion, winding and turning like snakes. And lo, what was that? One of the snakes grabbed its own tail and the image whirled mockingly before my eyes. I came to my senses as though struck by lightning; this time, too, I spent the rest of the night working out the results of my hypothesis."

Friedrich Kekulé, on his discovery of the molecular structure of benzene (Translated in Rothenburg, 1998).

1 Introduction

Recent years have seen a surge in research examining relationships between memory and sleep. But despite a wealth of findings clarifying the roles of stages 2, 3 and 4 NREM and stage REM sleep in memory consolidation, our knowledge of the first stage of sleep, NREM stage 1 (NREM1), in relation to memory processes is lacking. As a brief, transitory state, NREM1 sleep may seem trivial or uninteresting; however, it is characterized by a highly dynamic brain state whose neurophysiology is likened by some to a hybrid of wake, NREM and REM sleep (see Table 1). For example, recent studies (Bódizs, Sverteczki, Lázár &

Halász, 2005; Bódizs, Sverteczki & Mészáros, 2008) have shown hippocampal activity during NREM1 that is characteristic of REM sleep. Rather, the impediment to studying NREM1 sleep is that it is the gateway to sleep and thus it does not lend itself well to current experimental paradigms that have been fruitful in investigating the role of sleep for learning and memory in humans. Nonetheless, one study (Lahl, Wispel, Willigens & Pietrowsky, 2008) found enhanced retention of word lists after 5 min naps containing minimal amounts of stage 2 sleep, leading the authors to suggest that the task was processed during NREM1.

—Insert Table 1 About Here—

While studying memory processing during NREM1 may present particular challenges, its proximity to wakefulness makes it an ideal stage for probing the phenomenological contents of mental activity. Methods of collecting sleep mentation have recently been used to clarify learning and memory processes during NREM sleep (e.g., Wamsley & Antrobus, 2009; Wamsley, Perry, Djonlagic, Reaven, & Stickgold, 2010; Stickgold, Malia, Maguire, Roddenberry, & O'Connor, 2000), with one study (Wamsley, Tucker, Payne, Benavides, & Stickgold, 2010) finding a strong link between dreaming of a task in NREM sleep and increased sleep-dependent learning. These studies support the notion that mentation during NREM sleep reflects memory processing, and may provide a unique perspective by which offline memory processing can be examined (see Stickgold and Wamsley, 2009).

It is well known that vivid visual imagery is experienced at sleep onset—and only remembered if the individual is awakened at this time. Early studies examined this imagery specifically in terms of its similarity to REM sleep dreaming (Foulkes & Vogel, 1965; Foulkes, Spear, & Symonds, 1966; Vogel, Barrowclough, & Giesler, 1972; Foulkes &

Schmidt, 1983; Rowley, Stickgold & Hobson, 1998). More recent studies have either focused on the EEG correlates of sleep onset dreaming without considering its relationship to memory and learning (Germain & Nielsen, 1997; Hayashi, Katoh, & Hori, 1999; Hori, Hayashi, & Morikawa, 1993; Nielsen et al., 2005) or examined it in relation to a pre-sleep task without specifying EEG or other associated physiological correlates (Stickgold et al., 2000; Wamsley et al., 2010). The present study is an exploratory attempt to consider all of these factors together with a single, highly trained participant; i.e., to examine the imagery and memory processes associated with a sub-stage of NREM1 with distinct EEG correlates. The objective is to evaluate NREM1 dream reports for evidence of memory processing that may be active at this time, specifically, 1) the presence of hippocampally-mediated, declarative memories, and 2) chronological and semantic patterns of memory representation.

The target NREM1 sub-stage is one of nine EEG patterns first defined by Hori et al. (1993b) and illustrated in Table 1. Beginning with relaxed wakefulness characterized by alpha wave trains (sub-stage 1) and intermittent alpha >50% (sub-stage 2), a reliable sequence (Doerfling, Ogilvie, Murphy, & Lamarche, 1996) of sub-stages characterizes NREM1: intermittent alpha <50% (sub-stage 3), EEG flattening (sub-stage 4), theta waves (sub-stage 5), solitary humps or solitary vertex waves (sub-stage 6), hump trains or vertex waves (sub-stage 7), humps or vertex waves with incomplete spindles (sub-stage 8) and spindles (sub-stage 9). The latter sub-stage typically signals the onset of NREM stage 2 sleep.

Of particular interest to learning and memory is NREM1 sub-stage 5 (NREM1Φ), characterized by clearly visible low voltage theta waves, following which dream-like experiences are reported with very high frequencies (Germain & Nielsen, 1997; Hori et al., 1993; Nielsen et al., 2005). Cortical theta is reliably associated with learning and memory (see Mitchell, McNaughton, Flanagan, & Kirk, 2008 for review) and is involved with

declarative memory consolidation during REM sleep in humans (Fogel, Smith, & Cote, 2007). Importantly, theta is thought to underlie the interactions between hippocampus and neocortical areas (Buzsaki, 2006; Miller, 1991) that form the basis of episodic memory encoding and retrieval, i.e., the ability to re-experience an event in some perceptual detail (Tulving, 2002).

Dreaming has also been described as a function of hippocampal-neocortical interactions that are constrained and modulated by the unique neurophysiology of REM sleep (Johnson, 2005; Nielsen & Levin, 2007; Nielsen & Stenstrom, 2005; Paller & Voss, 2004; Payne & Nadel, 2004; Sil'kis, 2010; Stickgold, 2002; Stickgold, Hobson, Fosse, & Fosse, 2001). We have argued (Nielsen & Stenstrom, 2005) that the hippocampus plays a critical role in dream construction by binding neocortical memory traces together to create the "here and now" experience of dreaming. Consistent with evidence described earlier that REM-related processes such as hippocampal theta occur at sleep onset (Bodizs, et al., 2005; see Nielsen, 2000 for review) and that theta is associated with sleep onset imagery (Nielsen et al., 2005), we expect that hippocampal processes will also be involved in the theta-rich sub-stage of NREM1Φ dreaming.

The notion of hippocampal involvement in sleep onset imagery, and in dreaming more generally, is nonetheless contested. The seemingly chaotic and isolated nature of dreaming is taken by some authors to indicate that dream imagery is generated with an absence of hippocampal input (Payne & Nadel, 2004). Moreover, the finding that densely amnesiac, hippocampal-lesioned patients report sleep onset imagery similar to that of controls suggests that dreaming at sleep onset does not utilize the hippocampally–mediated declarative system (Stickgold et al., 2001).

The issue of hippocampal involvement in NREM1Φ has not been clarified by fMRI (Kaufmann et al., 2006; Picchioni et al., 2008) and MEG (Ioannides, Kostopoulos, Liu, & Fenwick, 2009) studies examining NREM1 because the NREM1 sub-stage has not been studied in isolation. Nonetheless, one fMRI study of NREM1 sleep found an increase of hippocampal activity from the first to the last 30 sec of the NREM1 period (Picchioni et al., 2008). It remains an open question whether this increase in hippocampal activity occurs before, during or after the theta bursts of sub-stage 5. Because the hippocampus and theta activity are central to memory processes, their co-activation at sleep onset would be consistent with a possible role for this stage in memory consolidation.

The current study explores a novel methodological approach to this question by probing specific phenomenological qualities of NREM1Φ imagery for evidence of processes that are known to be hippocampally mediated. Imagery was analyzed for the presence of *scene construction* (Hassabis & Maguire, 2007) a process shown to be critically dependent on the hippocampus (Hassabis & Maguire, 2009). The notion of scene construction as a hippocampally-mediated process rests on findings that patients with hippocampal lesions are severely hindered in remembering past experiences (Squire, Stark, & Clark, 2004) and imagining new situations (Hassabis, Kumaran, Vann, & Maguire, 2007). Similarly, fMRI studies with healthy participants demonstrate that the hippocampus is involved with recreating past experiences and imagining future experiences (Addis, Pan, Vu, Laiser, & Schacter, 2009; Addis & Schacter, 2008; Addis, Wong, & Schacter, 2007), as well as imagining fictive scenarios (Hassabis, Kumaran, & Maguire, 2007). Together these findings converge in demonstrating that the hippocampus is critically involved in scene construction, i.e., binding disparate elements of an imagined situation within a spatial framework (Hassabis & Maguire, 2007).

Accordingly, evidence of scene construction in NREM1Φ images would be consistent with hippocampal involvement at this time. While sleep onset imagery is claimed by some to be associated with isolated objects (Mavromatis, 1987; Stickgold et al., 2000), we have observed complex, spatially embedded, hallucinatory activity associated specifically with the NREM1Φ sub-stage in several subjects (unpublished findings). To further examine this effect, a participant trained in self-observation was awakened multiple times from discrete episodes of NREM1Φ sleep during two non-consecutive nights. The participant provided detailed reports of the immediately preceding imagery; these were assessed for the presence or absence of scene construction.

We also examined the temporal and semantic characteristics of memories that the participant associated to this imagery ('memory sources') as evidence of memory processing during NREM1Φ. Previous research has demonstrated a reliable temporal pattern of memory source incorporation into night dreams (for review see Nielsen, 2004) that is characterized by a predominance of memory sources from 1-2 days prior to the dream (day residue effect) and 5-7 days prior to the dream (dream lag effect) as compared to 3-4 days prior to the dream (Blagrove, Henley-Einion, Barnett, Edwards & Seage, 2010; Nielsen, Kuiken, Alain, Stenstrom, & Powell, 2004; Nielsen & Powell, 1989; Powell, Cheung, Nielsen, & Cervenka, 1995). The dream lag effect has been explained as due to cellular-level hippocampal memory consolidation processes (Nielsen & Stenstrom, 2005) and has not yet been investigated in sleep onset dreaming. Thus, the participant in the present study was required to provide detailed reports of potential memory sources of NREM1Φ dreams. On the assumption that REM-like processes occur during NREM1Φ, we predicted that the temporal pattern of dream incorporations previously found for REM sleep dreaming (day residue and dream lag effects) would also be found at sleep onset.

That REM processes occur during NREM1Φ may also indicate that imagery at this time will, in a manner similar to REM dreams (Fosse et al., 2003), not replay complete episodic episodes. While NREM stage 2 dreams contain a large number of episodic elements compared to SWS and REM sleep (Baylor & Cavallero, 2001), no study to date has examined the extent to which NREM1 dreams are characterized by the presence/absence of episodic replay. To address this, the present participant provided ratings of *episodic integrity*, defined as the degree to which each NREM1Φ dream consisted of a replay of a previous experience. We predicted that NREM1Φ dreams will not be episodic replays but, like REM sleep dreams, will consist of novel associations between distal memories.

Our specific hypotheses concerning the imagery reported following NREM1Φ awakenings were as follows:

H1) NREM1Φ dreams will be constructed as scenes, i.e., will contain items situated in a three dimensional environment forming a coherent scene, as opposed to items not well integrated within an environment or missing an environment altogether.

H2) Memory sources for NREM1Φ dreams will be influenced by similar temporal factors as sources for REM sleep dreams, i.e., the day-residue and dream-lag effects. Thus, memory sources will originate in events occurring 1 or 2 and 5, 6, or 7 days, as opposed to 4 or 5 days, prior to occurrence of the dream.

H3) NREM1Φ dreams will not consist of the replay of whole episodic memories but, like REM dreams, will feature multiple memory sources from unrelated memories.

2 Methods

A single male participant (author KF, age 23) in good mental and physical health was previously habituated to the laboratory environment, had good dream recall, and had not used medications, drugs or alcohol at least 1 month prior to the experiment. He had been practicing dream recall and identifying memory sources of his dreams several years prior to the first night. He previously underwent 2 sessions of NREM1Φ awakenings (5 and 10 awakenings each; not reported here) according to the methods described below. He was aware that an objective of the current study was to identify memory sources, and was aware of the day-residue and dream-lag effects, but was unaware of the hypothesis concerning scene construction.

The participant slept two non-consecutive nights in a sleep laboratory with EEG recordings made from C3, C4, O1 and O2 electrodes applied according to the standard 10-20 system. We awakened the participant repeatedly throughout the entire night between the hours of 11 PM and 7 AM and exclusively during NREM1Φ sleep, i.e., when at least 5 sec had elapsed of Hori sub-stage 5 characterized by low voltage theta (5-7Hz) wave ripples with an amplitude of 20 μV to 50 μV (Hori, Hayashi, & Morikawa, 1993a). The sleep stage was determined in real time by an experienced polysomnographer. When the stage criteria were met, the experimenter called the participant by his first name through an intercom preset at a comfortable volume.

The participant gave a detailed verbal report of each experience that had immediately preceded the call; he sometimes made drawings of the imagery for clarity. This report was followed by a report of any distinct memory sources he could identify for specific dream elements. A distinct memory source was defined as an object, person, setting or sound whose waking-life source the participant could unambiguously recall. He stated the approximate

time in days, months or years since that memory had occurred. Memory sources were later classified by the experimenter into one of 4 temporal bins: 0-3 days, 4-30 days, 1-11 months and 1 year or more.

The participant then verbally responded to scales measuring the presence of self (yes or no), perspective (first person, third person or both), self movement (yes or no), movement other than self (yes or no), presence of emotions (yes or no), intensity of emotions (1 to 9; 1 = not at all intense, 9 = extremely intense), valence of emotions (1 to 9; 1 = very negative, 5 = neutral, 9 = very positive), and type of emotion (open-ended). The participant also rated dream reports for the extent to which they reflect an actual memory, i.e., episodic integrity (1 to 9; 1 = not at all like a replay of a memory, 9 = entirely like a replay of a memory) and the extent to which the dream was bizarre (1 to 9; 1 = not at all bizarre, 9 = extremely bizarre).

Two days following each experimental night the participant and one author (PS) examined the dream reports to identify recurring elements, defined as semantically similar elements in the dream.

Finally, two independent judges, unaware of the study's hypotheses, evaluated the presence of scene construction in the dream; drawings made by the participant were also available for this task. Transcribed dream reports were classified into three bins: 1) presence of scene construction: imagery containing clear evidence of items well integrated within a three dimensional environment; 2) absence of scene construction: reports containing no evidence of items integrated within a three dimensional environment; and 3) ambiguous reports: imagery containing unclear evidence that items were integrated within a three dimensional environment. Items were defined as either an object or a person.

3 Results

The participant was awakened 16 times during Night 1 and 18 times during Night 2 for a total of 34 awakenings with reports. Three awakenings produced only 'thought-like' activity (i.e., no imagery) and were discarded. The remaining 31 reports contained hallucinatory activity (pseudo-sensory imagery) that defined 'dreaming' for the present study.

The participant reported himself as being awake for 44 % of awakenings, as sleeping for 28% and as "not sure" for the remaining 28% (ratios very similar to those obtained from 27 other subjects in our lab; unpublished data, see Table 1). A majority of awakenings gave rise to visual imagery (N = 31; 100%) composed of a three dimensional environment in which the participant was present (N = 24; 77%) and viewing the scene from a first person perspective (N = 24; 77%). In no case did the participant report seeing himself. While for about half of the reports the participant was engaged in motor activity (N=14; 45%), in most cases something in the environment was moving (N = 28; 90%). Emotions were present in most (N = 21; 67%) reports and were of generally low intensity (M = 3.90, SD = 1.70). A balanced mix of positive (N = 6, e.g., exhilaration of flying with a flock of geese) and negative (N = 5; e.g., fear of falling off a building; anxiety over another dream character being injured) emotions was reported.

3.1 Scene construction

The two judges agreed on the categorization of the imagery in regards to the presence of scene construction in all cases but three, and resolved the discrepancies after discussing the matter with the participant. In most cases (N = 26; 84%) dreams were judged to be constructed as scenes, i.e., objects were well integrated within a three dimensional environment. In only four dreams (13%) was there no evidence of scene construction

whatsoever: in one case there occurred an environment but no object (‘protagonist traveling through space’); in the 3 other cases (9%) an object occurred without an environment (e.g., ‘a cube floating in darkness’, the participant’s headphones appearing isolated from any environment). In two other cases (6%) the dream began with simple objects that evolved into 3D scenes (e.g., simple geometric shapes bouncing around becoming slowly integrated into a full scene); these were considered as examples of scene construction. In another case (3%) both an object and a background was present but there was insufficient information to determine whether they were well integrated within a three dimensional environment (e.g., an isolated white cube that seemed to have emerged from a body of water).

3.2 Episodic replay

Only one dream was described as highly episodic, i.e., the near replay of a past event, and even this dream contained discrepancies with the actual event. The event in question was the participant sitting on a ski slope with friends 1 month prior to the experiment (score: 9 out of 9 for episodic integrity). Dreams were described as containing varying degrees of episodic integrity, with an average rating of 3.81 (SD = 2.24) on the 1-9 scale. Four dreams contained no bizarre elements at all, with an average bizarreness score of 4.52 (SD = 2.47) on the 1-9 scale. Bizarreness scores were negatively correlated with episodic integrity scores (r_{30}=-.594, p = .0001) and positively correlated with the number of memory sources contained in each dream (r_{30}= .638, p = .0001). The number of memory sources negatively correlated with episodic integrity (r_{30}= -.363, p = .045).

3.3 Memory Sources

A total of 81 distinct memory sources were reported for 31 dreams; at least one memory source (and as many as 5) was identified for each dream, with an average of 2.6 (SD = 1.1) memory sources per dream. Six dreams (19%) produced memories from immediately prior to sleep (e.g., lab technician, EEG amplifier), 16 (52%) produced memories from within the last 3 days, and 16 (52%) produced memories from 1+ years ago (see Figure 1). The most distant source was 15 years ago. Surprisingly, not a single occurrence of memory sources from 4 to 13 days ago was reported.

Memory sources from immediately prior to sleep always occurred within the first four awakenings on both nights (N1, 11:32-12:58 AM; N2, 11:56-12:34 AM), while years-distant sources never appeared until at least the 4th awakening on Night 1 (12:58-5:41 AM) and the 3rd awakening on Night 2 (12:34-5:15 AM), suggesting that time-of-night/circadian factors influenced reported memory sources. Twenty-one dreams (67%) produced memories from the last 1-11 months, however, only 3 of these dreams produced memory sources exclusively from 1-11 months ago. The other 18 dreams produced additional memories from the last few days, from years ago, or from both. Six reports (19%) produced memory sources from both the last 3 days and more than 1 year ago.

3.4 Semantic elements

Recurring semantic elements (n = 18), ranging from general themes (e.g., China) to specific objects (e.g., a white cube), were identified for several dreams within a single night. In contrast, only 2 recurring elements (Buddhism and University) were found across the two nights, and these referred directly to ongoing, long-term concerns of the participant. Overall, recurring elements appeared in from 2 to 5 (M = 2.47, SD = .70) different dreams and could

be traced to specific memories 77% of the time (n = 14). When the memory sources of recurring elements could be identified, in all cases they could be traced to distinct and unrelated memories sometimes separated by several years. For example, the theme of 'outer space' recurred in 5 dreams on N1; memory sources were identified as three science fiction films seen 14 days, 8 months, and 3 years prior to the experiment, and two science-related books read 14 days and 3 months prior (see Table 2). The three films, for example (*2001: A Space Odyssey*, *Time Cop*, and *Fire in the Sky*), were viewed months or years apart, are totally unrelated to one another (e.g., not sequels, or featuring same director or actors), and were themselves produced over a period of nearly 30 years (1968 – 1994). Yet the common theme of futuristic technology and advanced forms of space-time travel was culled from all three films and recurred throughout a single night of NREM1 dreams alongside similar themes taken from books. Recurring elements were always distributed equally throughout the night, and were separated by an average of 3.82 (SD = 2.37) dreams between reappearances.

—Insert Table 2 About Here—

Recurring elements could also be found *within* single dreams. In 32% (n = 10) of dreams, memory elements with similar semantic properties yet stemming from different memories separated by from 2 days to 15 years appeared simultaneously in a single dream (see Table 3). In most cases (8/10), semantically related items came from memories that were separated by from 1 to 15 years (M = 4.21, SD = 5.03). The two remaining dreams were particular in that semantically related items stemmed from the same location (McGill University Campus); the dreams were only 10 minutes apart and the memories 3 months apart.

—Insert Table 3 About Here—

4 Discussion

To investigate the possibility that memory processing occurs during NREM1 sleep a trained participant was awakened 34 times from episodes of NREM1 sub-stage 5 sleep (with theta activity) across two non-consecutive nights for mentation reports. A majority of awakenings (31/34; 91.2%) resulted in detailed reports of vivid visual images that were constructed as integrated scenes and linked to a variety of memory sources.

4.1 Evidence of scene construction

A vast majority of recalled dreams (84%) was judged to be composed of multiple items (objects or persons) that were coherently integrated within a defined spatial context, i.e., a three-dimensional environment. They are thus similar in nature to other imaginative activity in which item-in-context associations are visualized as scenes, namely, remembering a past event (episodic memory), thinking about a future event, or imagining a novel event (Addis, McIntosh, Moscovitch, Crawley, & McAndrews, 2004; Addis et al., 2009; Addis & Schacter, 2008; Addis et al., 2007; Hassabis, Kumaran, & Maguire, 2007; Hassabis, Kumaran, Vann et al., 2007; Weiler, Suchan, & Daum, 2010). This type of scene construction is thought to reflect the hippocampally mediated process of binding together disparate neocortical traces into a coherent whole (Hassabis & Maguire, 2007, 2009) and, in this respect, our theta-linked NREM1Φ hypnagogic dreams may well be hippocampally mediated like these other forms of mentation.

This finding appears to contradict previous reports that densely amnesic patients with bilateral hippocampal lesions report imagery similar to that of controls during unspecified NREM1 or Stage 2 sleep (Stickgold et al., 2000). However, because in the latter study the reported imagery consisted of pre-sleep task-related Tetris blocks dissociated from any sort of environment, and thus did not involve scene construction as defined by Hassabis and Maguire (2007), the hippocampus need not have been involved in production of the imagery. In fact, because the theta ripples characterizing NREM1Φ are short in duration and account for only a fraction of each NREM1Φ episode, it is possible that previous studies investigating sleep onset cognition have not awakened participants at a time when the hippocampus was active. Indeed, sleep onset imagery is commonly described as containing isolated objects (Mavromatis, 1987) and it is possible that imagery during theta bursts is unusual in its complexity precisely because of involvement of the hippocampus.

While the structure of NREM1Φ dreaming was characterized by scene construction in much the same manner as episodic memory recall is, these dreams did not consist of replays of episodic memories. Instead, most were described as bizarre and as containing a wide range of elements relating to multiple memory sources. In fact, only 1 dream (3.2%) was considered highly episodic, and only 5 dreams (16%) were not considered bizarre, with most featuring moderate levels of bizarreness (4.5 on a scale of 1 to 9) and moderate levels of episodic integrity (3.8 on a scale of 1 to 9). Furthermore, the degree of episodic integrity was found to be negatively correlated with the degree of bizarreness and the number of memory sources identified in a dream. Along with the finding of a positive correlation between the number of memory sources and bizarreness, these results suggest that dreams of low episodic integrity containing a number of distal memory sources will, quite reasonably, be rated as bizarre.

4.2 Temporal aspects of memory sources

The predominance of recent memories during the first 4 awakenings and of distant memories from the 3rd awakening onward is consistent with previous findings that early-night REM dreams are constructed from more recent memory sources, and late-night REM dreams from more temporally distant sources (Verdone, 1965). This may indicate that either circadian or sleep-dependent processes underlie the recent/remote quality of memory source selection for both REM sleep and NREM1Φ dreaming and further supports the claim that sleep onset NREM imagery may be modulated by changes in REM propensity (see Nielsen, 2010 for review).

In most cases, multiple memory sources linked to single dreams were separated by at least one month (see Figure 1). The intriguing possibility that memory sources within a single dream are targeted predominantly on the basis of distal temporal relationships is suggested by 1) the preponderance of reports eliciting memories from *both* 1-11 months ago and some other time period (less than 4 days, more than a year ago) and 2) the negligible number of dreams with *only* 1-11-month-old memories.

—Insert Figure 1 About Here—

We expected to find peaks in dream memory sources arising from 1-2 days ago (day residue) and 5-7 days ago (dream lag) based on previous studies for nocturnal dreams (Blagrove, 2010; Nielsen, 2004). However, although a clear day-residue effect was found, with 16 reports (52%) containing a memory source from 1 day prior, there was a total absence of a dream lag effect (0%). In fact, there was a curious lack of any memory sources

from 5 to 13 days ago, suggesting an important difference between REM and NREM1Φ dream-incorporation mechanisms.

4.3 Recurring semantic elements

Unexpectedly, a large number of memory sources were found to be semantically related. Previously, Cippoli et al., (1988) found interrelated elements in stage 2 and REM dreams within single nights. Here we report that during multiple sequential NREM1Φ episodes recurring elements are often related on a semantic level and most of these elements can be traced to episodic memories.

Eighteen recurring semantic elements were identified, ranging from simple objects (e.g., obelisk), personal items (e.g., pet animals), and landmarks (e.g., Asian temples), to more general themes (e.g., torture). With the exception of two semantic elements relating to pervasive personal concerns (Buddhism, University life), recurring semantic elements were specific to a single night. For example, the semantic element 'science fiction' was present in 5 dreams distributed across Night 1 and entirely absent on Night 2 (see Table 2). The fact that elements recurring across several dreams are not grouped together but are well distributed across the night suggests that multiple instances of semantically related elements across multiple dreams are not simply a function of semantic priming.

A third of all dreams contained semantically related items from distal memories. These items were isolated from their original context, i.e., dissociated from the memory of the event of which the items are a part, and integrated together in a novel scene that was vividly perceived. This offline manipulation of memory items bears a resemblance to *integrative encoding*, the hippocampally-mediated process by which overlapping items from separate events "are integrated into a linked mnemonic representation" (Shohamy & Wagner,

2008, p. 378). While the hippocampus has been demonstrated to enable *associative inference* between overlapping elements of two events that were not experienced together (Greene, Gross, Elsinger, & Rao, 2006; Heckers, Zalesak, Weiss, Ditman, & Titone, 2004; Preston, Shrager, Dudukovic, & Gabrieli, 2004), Shohamy and Wagner (2008) demonstrated that overlapping elements from separate episodes are encoded to provide a rich network of associations that cut across multiple events. While these studies limit distinct episodes to the duration of the experiment lasting only a few hours, here we find merged in a single scene semantically related items from memories that occurred months to years apart and that arose in entirely different contexts. That evidence of this phenomenon occurred in a third of all reports suggests that NREM1Φ dreaming may be involved in linking common elements from memories spanning several years (the oldest memory source was a toy animal from 15 years ago that the participant had not thought of since that time).

4.4. Similarities between NREM1Φ sleep and REM sleep

A century after Freud observed that past events are readily incorporated into dreaming, it is still unknown why certain memories are selected for incorporation, why specific elements within these memories are targeted for incorporation and what role the incorporation of such elements may play in offline memory processing. Here we provide preliminary evidence that during NREM1 sleep with theta waves, memory sources are selected on the basis of both distal temporal relationships and proximal semantic relationships, a finding consistent with the hypothesis put forth by Walker & Stickgold (2004) that the recombination of previous memories during REM sleep facilitates novel inferences.

Indeed, both REM and NREM1Φ dreams seem to form links between loosely associated items. For example, previous research suggests that the REM sleep state is characterized by a cognitive bias towards employing weak, as opposed to strong, semantic associations (Walker, Liston, Hobson, & Stickgold, 2002). Similarly, one study found that REM sleep is associated with increased performance on a creativity task; specifically, it served to prime associative networks and integrate unassociated information (Cai, Mednick, Harrison, Kanady, & Mednick, 2009). Along the same lines, we find that a third of the NREM1Φ dreams featured semantically related items stemming from episodic memories that were separated by several years and bound together in spatial and temporal proximity within the imagery. Such modification of semantic information suggests that this stage of sleep may be involved in cross-episode integration on the scale of decades. These exploratory results thus provide evidence for the possibility that offline memory processes occur during NREM stage 1 sleep just as they do during REM sleep.

4.5 Study limitations

The study has some important limitations. First, the study was based on a single participant, and thus conclusions drawn from the findings are tentative and require replication. Second, theta activity at sleep onset was (by necessity) visually detected but not later confirmed by off-line spectral analysis. Notwithstanding these weaknesses, however, the successful use of a single trained individual to lay bare important features of memory processing in dreams constitutes an important proof of principal and paves the way for future group-level studies.

4.6 Use of trained participants for the study of dreaming

For this study, the finding of patterns within the temporal and semantic characteristics of memory sources was largely due to the excellent quality of the image reports and associated memory sources. We have previously argued for the need to employ trained participants to counter difficulties inherent in gaining access to subtle features of dream experience (Nielsen & Stenstrom, 2005). Although dreams can be difficult to remember, recent evidence suggests that remembering the details of dreams is a learnable skill. We demonstrated that providing participants with training to remember dreams and to identify their memory sources increases these abilities (Solomonova et al., 2008). The current study demonstrates that a motivated participant, habituated to laboratory awakenings and trained and practiced in recalling dreams and memory sources can produce well remembered and detailed dream reports, the analysis of which may lead to a more nuanced understanding of the mind in sleep.

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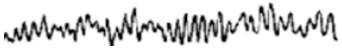
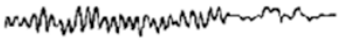
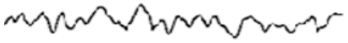
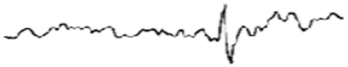
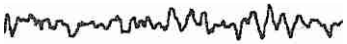
Table 1. Neurophysiology of NREM1 compared to NREM 2-3-4 and REM sleep and wakefulness.

Stage	sub stages[1]	EEG Signature	EEG Signature Waveform	Subjective State	Recall of Mentation	Eye movements	Hippocampal activity
Wake	1	Alpha wave train		Awake	?	?	?
	2	Alpha wave intermittent (>50%)		Awake	?	?	?
NREM 1	3	Alpha wave intermittent (<50%)		?	?	Slow and short lasting[2]	Diminished[5]
	4	EEG flattening (<20 μV)		Wake: 62% Sleep: 16% Not sure: 22%[10]	82%[10]	?	?
	5	Theta ripples		Wake: 43% Sleep: 40% Not sure: 17%[10]	85%[10]	Wake-like slow saccades[2]	?
	6	Vertex sharp wave (<200 μV)		?	?	Wake-like slow saccades[2]	?
	7	> 1 Vertex sharp wave (<200 μV)		?	?	Oculomotor slowing[2]	?
	8	Incomplete spindle		?	?	Oculomotor slowing[2]	Higher than wake[5]
NREM 2	9	Complete Spindle		Sleep	43%[11]	Minimal activity	Active[4]
NREM 3-4		Delta		Sleep	43%[11]	Minimal activity	Diminished[4]
REM		Theta		Sleep	82%[12]	Wake-like rapid	Active[6,7,8]

		saccades[3]	Higher than wake[9]

[1] Hori et al. 1994.; [2] Porte et al., 2004; [3] Ogawa et al., 2009; [4] Kaufmann et al. 2006; [5] Picchioni et al. 200; [6] Only PET data available for this area in REM; [7]Maquet et al. 1996; [8] Nofzinger et al. 1996; [9] Braun et al. 1997; [10] Unpublished findings from 104 Hori sub-stage 4 and 135 Hori sub-stage 5 reports from 27 healthy participants (Nielsen et al. 2005); [11] Nielsen, 2000 (average from 29 studies); [12] Nielsen, 2000 (average from 33 studies).

Table 2. Example of a recurring science fiction theme spanning multiple dreams on Night 1.

Time of awakening	Memory source	Semantic aspects of memory sources	Temporal aspects of memory source
12:22 AM, Dream # 3	Situation and environment from the movie "2001: A Space Odyssey (1968)"	Particular type of high speed space travel	Movie seen 14 days ago
03:09 AM, Dream # 10	Situation and environment from the movie "Fire in the Sky (1993)"	Examination by aliens in space ship	Movie seen 8 months ago
04:55 AM, Dream # 14	Objects from the movie "Time Cop (1994)"	Particular shape of time travel portal	Movie seen 3 years ago
05:22 AM, Dream #15	Environment from book "The Mind's Eye (2005)"	A virtual grid superimposed on a moonscape	Book read 14 days ago
05:41 AM, Dream #16	Object from comic "Battle Angel"	Particular shape of space ship	Comics read 3 months ago

Note: All space themes occurred during Night 1; no space theme occurred during Night 2.

Table 3. Examples of semantically related elements within a single dream

Time of awakening	Common Semantic Element	Description of elements included in the dream	Temporal aspects of memory source
Night 1 Dream #10 3:09AM	Body modification. Participant was on an operating table in a situation with visual and scene elements from 3 movies.	Body reconstruction from the movie "The Fifth Element (1997)"	2 months ago
		Autopsy from the movie "Fire in the sky (1993)"	8 months ago
		Torture from the movie "The Cell (2000)"	6 years ago
Night 2 Dream #13 4:00AM	Pets. Three pets from 3 time periods present in the backyard of childhood home.	Pet cat	2 months ago
		Pet rabbit	12 years ago
		Teddy bear	15 years ago

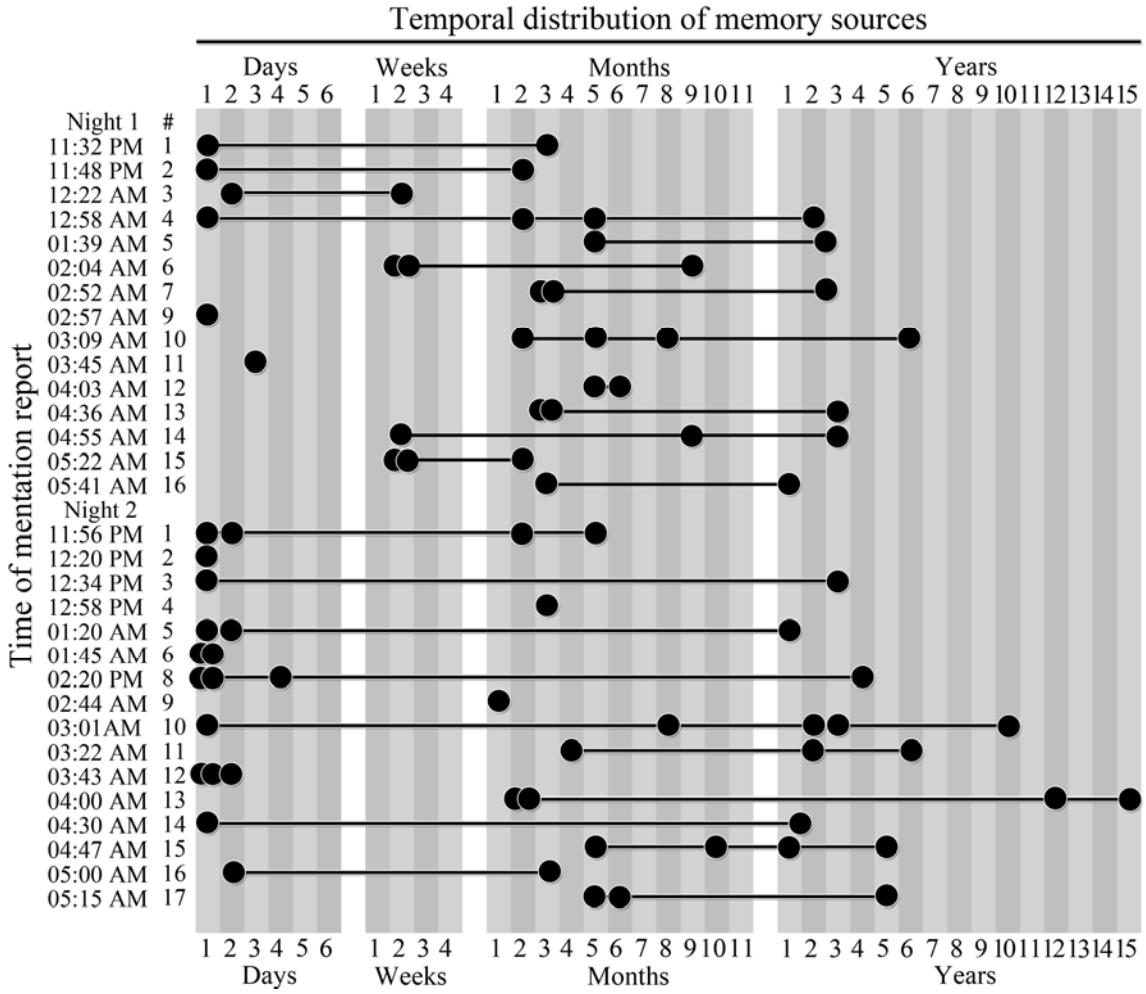


Figure 1. Temporal characteristics of memory sources pertaining to sleep onset mentation reports. Circles represent memory sources situated in time (X axis) for mentation reports occurring across two nights (Y-axis). Black lines connecting circles indicate sources are from the same dream.

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CHAPTER IV

Thinking during REM and Stage 2 sleep: dissociation of the production and validation of logic

Article IV - Thinking during REM and Stage 2 sleep: dissociation of the production and validation of logic

Author Contributions

PS and TN conceived and designed the experiment and wrote the paper. PS performed the experiment and PS and ES analyzed the data.

Thinking during REM and Stage 2 sleep: dissociation of the production and validation of logic

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Abstract

In his celebrated *Discourse on Method*, Descartes struggled with the notion of differentiating thinking in dreaming with that of the waking state. 400 years later, and despite numerous investigations of dream cognition, the question of how thinking is modulated across sleep-wake states remains poorly understood. Here we compare prefrontal and parietal brain regions that may be deactivated in REM and Stage 2 (S2) sleep with characterizations of the neural substrates of distinct phases of the reasoning process. Overlap between areas deactivated in REM sleep and those responsible for validation logic—but not for the production of logical thinking—leads to the hypothesis that during REM sleep dreaming the ability to think logically will be maintained while the ability to verify whether or not logical relationships in the dream scene are valid will be diminished. Laboratory awakenings and mentation sampling from REM and S2 sleep provide evidence that confirms the hypothesis and suggests that the production and validation of logic are dissociable and that such a dissociation characterizes cognition during these stages of sleep. Analysis of targeted mentation reports reveal that dream bizarreness has its basis in both violations of logic and novel item-context associations, the appreciation of which are dysfunctional in dreaming as predicted by sleep-specific modulations of fronto-parietal and hippocampal functioning, respectively. The results suggest a novel explanation of what makes thinking in dreaming similar to, yet so different from, thinking in the waking state.

Does our ability to engage in logical thinking survive the important modulations of brain activity that occur in sleep? On the one hand, hypoactivation of the dorsal lateral prefrontal cortex (DLPFC) during REM sleep (Braun et al., 1997; Maquet et al., 1996) is interpreted by some authors (Hobson, 2004; Hobson, Pace-Schott & Stickgold, 1998; Muzur, Pace-Schott & Hobson, 2002) to support the claim that illogical thinking occurs during REM sleep dreaming. On the other hand, recent evidence that logical thinking is readily found in dream reports (Wolman & Kozmova, 2006) echoes observations from early investigators that in dreams we have wake-like thoughts (Aristotle, 350 BC) and that these thoughts are rational (Descartes, 1637).

Here we draw upon recent clarifications of the neurophysiology of sleep as well as recent descriptions of brain areas implicated in thinking and the detection of contextual novelty to revisit the question of whether and how logical thinking is modulated across sleep-wake states. At the heart of our hypothesis is the notion that different aspects of thinking are differentially modulated in sleep consciousness, as hinted at in a study reporting that thinking *within* the hallucinatory context of the dream is similar to waking-state thinking (i.e., rational), while thinking *about* the scenario itself is not (Kahn & Hobson, 2005).

Logical validation and DLPFC hypoactivation

A recent meta-analysis of PET imaging results comparing waking and REM sleep states (Maquet et al., 2005) has revealed hypoactivation, during REM sleep, of specific areas within the parietal lobes and the DLPFC and other prefrontal regions. A combined EEG and fMRI study found a somewhat similar pattern of activation in Stage 2 (S2) NREM sleep (Kaufmann et al., 2006). Here we focus on regions of sleep-specific hypoactivation which overlap neural areas associated with logical thinking.

Tasks involving deductive logic are typically associated with wide patterns of activation within frontal, parietal, temporal, occipital, basal ganglia and cerebellar regions (Goel, 2007). While the cerebellum, basal ganglia, temporal and occipital areas associated with logical thinking are active in both REM and S2 sleep, most of the prefrontal and parietal areas are deactivated at this time. Specifically, during REM

(Maquet et al., 2005) and S2 (Kaufmann et al., 2006) sleep there is selective deactivation of the inferior frontal gyrus (IFG) and the middle frontal gyrus (MFG), both of which are implicated in logical deduction (Goel & Dolan, 2003; Goel & Dolan, 2004), logical induction (Goel & Dolan, 2004) and analogical reasoning (Luo et al., 2003). There is also deactivation of the inferior parietal lobule, which is associated with logical deduction and induction (Goel & Dolan, 2004).

Although these activity decreases suggest that the brain states of REM and S2 sleep are not conducive to rational thinking, a recent study (Fangmeier, Knauff, Ruff & Sloutsky, 2006) that examined specific patterns of brain activation associated with three hypothesized phases of deductive reasoning suggests that regions of sleep-specific hypoactivation overlap almost exclusively with brain areas involved in the third and final phase of this reasoning paradigm, i.e., the validation phase. The validation phase of reasoning takes place when participants decide if the conclusion they had previously drawn from the premises given matches the conclusion currently displayed on a computer screen. In contrast to the validation phase, brain regions involved in the processing of a premise, e.g., V = X, in the integration of a second premise, e.g., X = Z, and in the hypothetical production of a putative conclusion, e.g., V = Z, are similarly active in REM and waking state (see Table 1 for details). In S2 sleep, only 6 of 8 regions implicated in the integration phase are active; the left parahippocampal gyrus and the left anterior cingulate show less activity in S2 than during the integration phase of waking reasoning.

Together, these findings suggest that in REM, and to a less extent in S2 sleep, regions associated with the integration of premises and the production of a putative conclusion remain active whereas regions associated with evaluation of the validity of this putative conclusion (validation) do not.

---Insert Table 1 about here---

Based on findings such as these, it seems likely that cognition during REM sleep dreaming is characterized by occurrences of logical reasoning for which validation of putative conclusions is deficient. This proposal leads to two predictions about the characteristics of REM sleep cognition: 1) participants will report thinking logically

during dream events, and 2) participants will not verify whether logical relationships in the dream scene are valid or not. Some evidence supports these predictions.

First, that logical thinking occurs in dreaming is consistent with a recent study reporting a wide variety of categories of rational thought, such as analytical thinking, in dream reports (Wolman & Kozmova, 2006). These findings question some authors' descriptions of thinking in REM sleep as illogical or suffering from tenuous logic (e.g., Hobson, 2004; Muzur et al., 2002). However, no study has yet examined logical rigor in dreaming cognition by means of controlled laboratory awakenings and targeted probes.

Second, that putative conclusions derived from reasoning are not verified during dreaming corresponds to the generally accepted but little investigated characteristic of dream cognition that dreaming individuals are unable to appreciate bizarre qualities of their hallucinatory environments—no matter how illogical or impossible they may be. In dreams, "persons, times, and places are fused, plastic, incongruous and discontinuous" (Hobson, Pace-Schott & Stickgold, 2000). Dream bizarreness occurs in a majority of REM sleep dreams (Natale and Esposito, 2001; Rittenhouse et al., 1994) although its definition varies considerably. For example, bizarreness has been defined as "events outside the conceivable expectations of waking life" (Snyder, 1970), as "violations of real-world rules" (Cicogna, Occhionero, Natale & Esposito, 2007) or as unusual combination of features in the binding of different information sources (Revonsuo and Tarkko, 2002).

While the scope of bizarreness during dreaming may be considerable, we propose that the curious absence of awareness about it may be understood, at least in part, as a failure to validate the logical coherence of dream events which, in turn, results from a sleep-specific hypoactivation of the brain regions responsible for logical validation during reasoning.

Context novelty and hippocampal dysfunction

A second set of findings concerning impaired hippocampal functioning also has implications for the phenomenology of dream thought. From this literature it can be argued that some dream bizarreness may be viewed more as a violation of context than a violation of logical premises *per se*. For example, dreaming of a clown in a lecture hall might be considered bizarre because of a violation of expected context, not because

the clown, the lecture hall or the relationship between the clown and the lecture hall constitutes a violation of logic. Indeed, it is possible that the bizarre nature of some dreams may be understood as a novel juxtaposition of items within a context. The detection and encoding of contextual novelty, defined as an event or stimulus that is unexpected given the context in which it occurs (Kumaran & Maguire, 2007), is dependent on the hippocampus (Halgren et al., 1980; Knight, 1996; Strange et al., 2000; Strange and Dolan, 2001; Kishiyama et al.,2004; Yamaguchi et al., 2004; Harrison et al., 2006), a brain area whose functioning is heavily modulated in REM sleep (Montgomery et al., 2008; Sil'kis, 2009). The role of the hippocampus in the detection of novelty is believed to rest upon the ability of the CA1 region to compare incoming sensory information from the cortex with stored representations from DG-CA3 networks (Hasselmo and Schnell, 1994; Lisman & Otmakhova, 2001). The hippocampus then generates a match/mismatch signal based on overlap between memory-based predictions of the DC/CA3 networks and sensory reality signals from the entorhinal cortex. A recent study found diminished gamma and theta coherence between CA1 and DG-CA3 networks during REM sleep (Montgomery et al., 2008), suggesting that the ability of hippocampus to function as an item-context novelty detector may be diminished in REM sleep on the basis of modulated communication between CA1 and DG/CA3 areas. It is therefore likely that during REM sleep bizarre elements resulting from novel item-context will not be appreciated or understood as bizarre by the dreamer.

In sum, new observations concerning the functional deactivation of prefrontal and parietal regions, as well as altered processing of the hippocampus during REM sleep provide a basis for explaining how some aspects of logical reasoning and the ability to detect unusual features of the environment may be modulated across sleep-wake states.

While in REM sleep diminished neural activity is confined to areas involved in the *validation phase* of Fangmeier et al.'s (2006) logical reasoning paradigm, in S2 sleep an additional diminishment of activity is observed in some brain regions involved in the *integration phase* (see table 1). It is therefore likely that the ability to detect illogical aspects of dream bizarreness will be similar across REM and S2, whereas

thoughts in S2 sleep mentation will be characterised as containing less logical rigor than thoughts in REM sleep mentation.

Because data on cellular-level activity in the hippocampus during S2 is lacking, it is unclear whether diminished CA1-DG/CA3 communication seen in REM, hypothesized here to underlie the ability to detect novel context-item associations, also occurs during S2. Nonetheless, in line with the covert REM hypothesis (Nielsen, 2000), which posits that REM processes within NREM stages underlie NREM dreaming, and considering the important role of the hippocampus in dreaming (Nielsen & Stenstrom, 2005), we expect REM-like modulations of the hippocampus during S2 dreaming. We therefore expect a diminished ability to detect bizarreness characterised by novel item-context associations during S2 as well as REM dreaming.

The specific hypotheses are that:

H1) In REM sleep, the logical rigor of thinking will be high;

H2) Logic rigor of thinking will be greater in REM than in S2 sleep;

H3) In REM and in S2 sleep, the ability to appreciate bizarre features will be low,

H4) Dream bizarreness will relate to both illogical elements as well as novel item-context associations (i.e., context novelty) within the dreamed environment for both REM and stage 2 mentation.

However, phenomenological observations pertaining to the modulation of logical reasoning during dreaming—in this case whether dream cognitions are predominately logical or illogical, and whether or not the illogical nature of dream bizarreness is appreciated—are lacking. The extent to which dream bizarreness has its basis in violations of logic or unusual item-context relationships is also unknown. To address these issues, we awakened participants from REM and S2 sleep and had them assess their dream cognitions immediately for a) the presence and nature of bizarreness, b) the degree to which bizarreness was appreciated, and c) the degree to which they were thinking logically during the dream.

Methods

Participants

Thirteen female and 1 male participants aged 21-32 years (M=23.4±6.2) were recruited by advertisement. They reported having no history of neurological and psychiatric disorders, or substance abuse, and all reported being free of sleep and dreaming disturbances. The experiment was approved by the ethics committee of Sacré-Coeur Hospital. Written and verbal consent was obtained from all participants who were compensated $75 for their time.

Polysomnographic recordings

All participants were instructed to avoid drinking caffeine and taking naps on experimental days. After arriving at the laboratory, they were situated in an acoustically isolated, electrically shielded room containing a single bed. The polysomnograph and other controls were housed in an adjacent control room where an experimenter was present at all times. An infrared video camera and microphone ensured that participants were monitored visually and acoustically at all times. Sleep recordings were performed with a 16-channel montage that sampled the electroencephalogram (EEG) at a frequency of 256Hz using international 10–20 electrode placements C3, C4, O1 and O2 (referred to A1 and re-referenced offline to linked ears), eye movements (two channels each for horizontal and vertical eye movements), electromyogram (2 submental and right tibialis EMG), oral-nasal airflow, and electrocardiogram. Recordings were performed using Harmonie version 4.1 (Stellate Systems, Montréal, Québec, Canada) and were scored for sleep stages manually according to Rechtschaffen and Kales (1968) criteria by an experienced polysomnographic technician who had not conducted the sleep recordings and who was blind to the purposes of the study.

Procedures

Participants spent 3 nights in the laboratory including an adaptation night for habituation to the laboratory. Nights 2 and 3 involved 4 awakenings each per night, for a total of 8 awakenings, half from REM sleep and half from S2 sleep. Awakenings were conducted both early (2^{nd} or 3^{rd} cycle) and late (4^{th} or 5^{th} cycle), and were counterbalanced across participants. Awakenings took place using a 500Hz 80dB 0.5-

second tone after 10 minutes of S2 or REM sleep had elapsed. After awakenings, the experimenter communicated immediately with the participant by intercom to collect a verbal mentation report and his/her ratings of this mentation.

Content rating scales

Upon awakening, participants were told: "Please describe what was going on in your mind before the tone". If no mental activity could be recalled, they were instructed to try to remember any mental activity for 5 minutes, after which they could go back to sleep. After describing their mentation, they verbally responded to probes concerning specific attributes of the mentation. Alpha activity was closely monitored on the EEG at this time to ensure that subjects remained awake. Responses were recorded on tape and later transcribed. To avoid 'secondary elaboration' and other demand characteristics (Revonsuo & Salmivalli, 1995), participants were also asked to rate various perceptual and emotional features of mentation (e.g., visual intensity) in addition to the cognitive variables of interest. Prior to the 1st experimental night, participants were given detailed instructions about the scales by the principal investigator to ensure that they fully understood the features being measured. Bizarreness was described to participants as "events, situations, people or objects outside the conceivable expectations of waking life", a definition loosely based on Snyder (1970). The questions pertaining to the variables of interest were:

1.1: Did you have any thoughts in your experience? *Yes/No*

1.2: How logical were your thoughts? *1 (not at all logical) to 9 (very logical).*

1.3: Did your thoughts relate to something in the dream? *Yes/No*; What was it? *Open-ended*

2.1: To what extent was your experience bizarre? *1 (not at all bizarre) to 9 (extremely bizarre)*; What was bizarre? *Open-ended*

2.2: During your experience, at what point were you aware that it was bizarre? *1 (not at all aware) to 9 (fully aware)*

For each participant, scores from multiple awakenings were averaged to produce mean scores. For yes/no type questions, "no" responses were coded as 0 and "yes" responses as 1. Paired t-tests were used for all comparisons unless otherwise mentioned. Only reports in which an experience with mentation (defined as presence of hallucinatory or cognitive activity) was identified were used in the analyses. Similarly, only instances for which bizarreness was present were included in the analyses pertaining to extent of awareness of bizarreness. Mentation reports were recorded and transcribed. An independent judge categorized the mentation reports containing bizarreness into four categories: 1) bizarreness relates to a violation of logic (e.g., defying the laws of physics, distortions of shape or size (see Cicogna et al., 2006) that defy logic, 2) bizarreness relates to a novel item-context relationship (the relationship between the item and the context is novel and unusual, and not the item or context *per se)*, 3) bizarreness relates to another factor not included in categories 1 or 2, and 4) the mentation report lacks sufficient information to properly categorize within the previous three categories. Categories 1 to 3 were not considered mutually exclusive.

Statistical analysis

Group scores were compared with T-tests unless otherwise noted. Because some participants did not report mentation or scores for target variables (particularly in S2), the number of participants included in each analysis is as follows: REM bizarreness (N = 13), S2 bizarreness (N = 8), REM logical thinking (N = 10) and S2 logical thinking (N = 8).

Results

In total, 86 awakenings were conducted, 55 (64%) of which contained mentation (38 REM, 88%; 17 S2, 38%). Forty-nine reports contained visual hallucinations (35 REM; 14 S2) and 21 contained thinking (14 REM; 7 S2).

Thinking

As predicted by hypothesis 1, a one sample T-test revealed that ratings of logical rigor for S2 and REM (M = 8.30, SD = 1.12) were significantly higher than the middle value of the scale (5.00; $t(8) = 10.11$, $p = .001$). Thoughts were considered very logical

(7, 8 or 9 out of 9) in 19 cases (91%), with the remaining 2 cases (9%) scored 5 and 6 (see Table 2).

Contrary to hypothesis 2, no difference was found between REM and S2 mentation for the presence of thoughts (REM: M = 0.60, SD = 0.32; S2: M = 0.66, SD = 0.37; $t(8) = .676$, $p = .51$) or the logical rigor of thoughts (REM: M = 8.42, SD = 1.20; S2: M = 8.06, SD = 0.94; $t(5) = .55$, $p = .606$). Out of 21 reports containing thinking, 19 (90%) also contained visual hallucinations. When hallucinations and thoughts co-occurred, participants reported that their thoughts were related to the visual hallucinations in 18 of 19 cases (94%).

---Insert Table 2 about here---

Bizarreness

Of the 49 reports with content, 35 (71%) contained some degree of bizarreness. As shown in Table 2, there was a large variability in the degree to which participants characterized their dream as containing bizarre elements. Of the 35 reports containing bizarreness, for 18 (51%) no awareness of this bizarreness during the dream was reported, and for only 2 (6%) was the bizarreness fully appreciated. In accordance with hypothesis 3, a one sample t-test revealed that ratings of awareness of bizarreness (M = 2.70 SD = 2.27) were significantly lower than the middle value of the scale (5.00; $t(11) = .-3.64$, $p = .003$).

No stage differences were found for the degree of bizarreness (REM: M = 3.94, SD = 1.61; S2: M = 3.14, SD = 2.53; $t(6) = .640$, $p = .546$) or the degree of awareness of bizarreness (REM: M = 2.46, SD = 1.72; S2: M = 3.46, SD = 3.22; $t(6) = -.471$, $p = .670$). For all 49 mentation reports containing visual content (100%), participants reported not being aware that they were dreaming.

Of the 35 dreams rated as bizarre, dream bizarreness was judged to be the result of both a violation of context and of logic in 9 cases, a violation of logic alone in 4 cases, and a violation of context alone in 16 cases (see table 3). In 6 cases the participant did not give sufficient information to properly evaluate the nature of the bizarreness. There was not a single case where the judge felt that neither violations of logic or context could properly explain the nature of the dreamed bizarreness.

Discussion

The results demonstrate a sleep-specific dissociation in cognitive ability in which the ability to think logically is maintained while the ability to critically examine illogical features and appreciate the novelty of item-in-context relationships within the hallucinatory environment is diminished. Participants awakened from REM and S2 sleep characterized their thinking during dreaming as logically sound while, at the same time, reported a diminished ability to appreciate the illogical nature of the dream events. These findings suggest that cognition in these stages of sleep is characterized by a dissociation between the production of logic (the ability to generate logical thoughts) and the validation of logic (the ability to evaluate whether something is logical or not).

Because a specific aspect of logical thinking was found to be diminished during REM and S2 dreaming, brain areas known to be deactivated at these times may be associated with this particular deficit of logical thinking. REM (Maquet et al., 2005) and S2 sleep (Kaufmann et al., 2006) are characterized by the deactivation of prefrontal areas associated with logical thinking tasks, namely the MFG (Goel et al., 2003; 2004; Luo et al., 2003) and IFG (Goel & Dolan 2003; 2004; Parsons & Osherson, 2001; Luo et al., 2003). Fangmeier et al., (2006) examined the neural correlates of three temporally separable phases of a logical deduction task and found the MFG to be involved specifically in evaluating logical statements as true or false. Similarly, the IFG is associated with evaluating anomalous information; for example, the left IFG is implicated in evaluation of sentences with conceptual (vs. syntactic) anomalies (Kuperberg et al., 2003), anomalous (vs. conventional) metaphors (Ahrens et al., 2007), nonsense (vs. literal or metaphorical) sentences (Stringaris et al., 2007) and anomalous information in an arithmetic task (Chen et al., 2007). Because dream bizarreness commonly involves both an anomaly of information and a violation of logic, deactivation of the IFG and MFG in REM and S2 sleep offers a parsimonious neurophysiological account of the diminished ability to process (i.e., become aware of) bizarreness in sleep mentation. Despite this reduction in cognitive ability, however, brain regions found by Fangmeier et al. (2006) to be involved in the production of logical conclusions, i.e., the processing and integrating of premises into a single unified conclusion, remain active in REM and S2 sleep and thus likely allow the dreamer to

think logically (see Table 1). The unusual (and seemingly paradoxical) dissociation in cognitive ability suggested by the current results is thus explained, at least in part, by the unusual pattern of cerebral activity known to characterize sleep (see Figure 1).

---Insert Figure 1 about here---

Bizarre features in the environment were not only described as violations of logic (51%) but also as unusual item-in-context associations (86%) and often as a combination of both (55%) (see table 3 for examples). In all cases (excluding 6 cases that lacked sufficient information to rate), dream bizarreness could be adequately explained by either violations in logic or unusual item-in-context associations, suggesting that most dream-related bizarreness adequately fits within these two dimensions.

While sleep-related prefrontal and parietal deactivations may account for the diminished ability to appreciate violations of logic, we further speculated that sleep-related modulations in hippocampal activity underlie a diminished ability to appreciate the novelty of unusual item-in-context relationships. While the types of novelty detection that are attributed to the hippocampus are still debated (see Kumaran & Maguire, 2007, for review), there is compelling evidence indicating a critical role for the hippocampus in detecting and encoding contextual novelty, i.e., an event or stimulus is unexpected given the context in which it occurs (Halgren et al., 1980; Knight, 1996; Kishiyama et al., 2004; Yamaguchi et al., 2004; Harrison et al., 2006). It is believed that the unique circuitry of the hippocampus enables it to compare ongoing sensory experiences with stored representations of past experiences (Hasselmo and Schnell, 1994; Lisman and Otmakhova, 2001). According to this view, the CA1 region of the hippocampus receives two inputs from the entorhinal cortex: 1) a direct connection representing actual sensory information from associative areas of the cortex and 2) information that has passed through recurrent networks of the DG and CA3 hippocampal areas responsible for representing associations previously encoded. The CA1 region thus carries out critical evaluations of overlap between stored representations and ongoing sensory information, with mismatches indicating contextual novelty. However, a study by Montgomery et al., (2008) found that during REM sleep theta and gamma coherence between the CA1 area and DC/CA3 networks is

reduced. We thus suggest that the partial isolation of CA1 from DC/CA3 networks observed in REM sleep may explain the current finding of a diminished appreciation of dream bizarreness that is rooted in contextual novelty.

As for hippocampal activity in stage 2 sleep, very little is known because studies have focused primarily on REM and slow wave sleep (e.g., Montgomery et al., 2008). However, one study has shown that the hippocampus shows greater activation during stage 2 sleep than either SWS or NREM stage 1 sleep (Kaufmann et al., 2006), suggesting an activation comparable to that in REM sleep. The current finding of a diminished ability to appreciate contextual novelty in both stage 2 and REM sleep is thus consistent with the possibility that hippocampal functioning underlying contextual novelty detection is modulated during stage 2 sleep dreaming in a manner similar to that during REM sleep dreaming.

In sum, previous research has shown that fronto-parietal areas may underlie violations of logic, while hippocampal circuits may underlie violations of context. Here we show that dream bizarreness appears to consist exclusively of violations of either logic or context or both, and that participants report a diminished ability to detect these violations of logic and context while dreaming in a manner predicted by sleep-dependent modulations of fronto-parietal and hippocampal areas.

This particular constraint on cognition during dreaming may allow a unique processing of information by which novel situations and stimuli are readily considered and acted upon regardless of how improbable, bizarre or illogical they may be. Numerous artistic endeavours and scientific breakthroughs are attributed to dreams (Maquet & Ruby, 2004) and perhaps our nightly bouts of extreme open-mindedness, in the face of hallucinatory environments that bind multiple memory sources into a constant flow (Nielsen & Stenstrom, 2005), may underlie the relationship between dreaming and creativity. How the unique cognition of REM and S2 sleep may be conducive to divergent thinking is illustrated in Figure 1.

Absence of sleep stage differences in logical thinking

In addition to the patterns of frontal and parietal deactivation characterizing REM sleep (Maquet et al., 2005), S2 sleep also features the deactivation of two brain areas (left anterior cingulate, left parahippocampus; Kaufmann et al., 2006) associated

with the integration of premises to generate a logical conclusion (Fangmeier et al., 2006). We therefore hypothesized that S2 sleep thinking would be characterized by less logical rigor than would REM sleep thinking whereas thinking in both states of sleep would be similarly deficient in appreciating illogical elements within the dream. The results demonstrate that while the ability to detect the illogical nature of dream bizarreness is, in fact, equally diminished in both S2 and REM sleep, contrary to our expectations the logical rigor of thoughts is similarly high in both stages. This may be due to the fact that the S2-specific deactivations of brain regions implicated in the "premise integration" phase of Fangmeier et al.'s (2006) paradigm (see Table 1 for details) is limited to 1) the left anterior cingulate, thus perhaps leaving the right anterior cingulate to compensate, and 2) the left parahippocampus, which may reflect the spatial nature of Fangmeier et al.'s (2006) experimental paradigm and not logical processing *per se*. However, interpretation of these results is limited by the small number of S2 reports.

Implications for state-dependent thinking

The notion of a sleep-specific dissociation between the maintained ability to produce logical thinking and the decreased ability to evaluate the illogical nature of bizarre elements, as predicted on the basis of known functional neuroanatomy and its modulation in REM and S2 sleep, provides a novel neurocognitive explication as to how dreaming is similar to, yet also different from, waking cognition.

The current findings nuance the controversy over whether thinking in REM sleep is logical or illogical. Indeed, because the validation of logic is deficient in REM sleep it is understandable why some authors, focusing on the delusion-like aspects of dream cognition, conclude that thinking is illogical in dreaming (Hobson, 2004; Muzur et al., 2002). At the same time, that the production of logic is functional in REM sleep explains why others have found evidence of rational thinking in dream reports (Wolman & Kozmova, 2007). Additionally, the observed sleep-specific diminishment in bizarreness detection may explain discrepant results in the literature concerning the extent to which cognition is modulated across mind-brain states. Studies supporting the idea that certain aspects of sleep cognition are wake-like (Kahan, 1994; Kahan, LaBerge, Levitan & Zimbardo, 1997; Purcell, Mullington, Moffitt, Hoffmann & Pigeau,

1986) have focused on cognitive accomplishments during dreaming and thus have not measured the ability to appreciate bizarreness. In contrast, studies supporting the view that cognition in dreaming is deficient (Hobson, Hoffman, Helfand & Kostner, 1987; Scarone et al., 2007; Renvonsuo & Salmivalli, 1995) may well have confounded measurement of the ability to detect bizarreness with other measurements of cognition. These authors conclude that thinking in dreaming is characterised by "cognitive bizarreness," but it remains unclear what specific elements of thinking are bizarre. For example, in the Hobson et al., (1987) and Scarone et al., (2007) studies, bizarreness of thought and bizarreness of the dream environment are not independently measured. As demonstrated by the present results, this distinction is critical: thinking during dreaming seems only to be bizarre in that the thinker cannot appreciate the bizarreness of the hallucinatory environment. The current study therefore underscores the importance of considering dream *imagery* (i.e., the hallucinatory environment perceived by the dreamer) and dream *cognition* (i.e., the internal thoughts of the dreamer during the dream) as separate in the same way as the environment and cognition are separate in waking life. For example, because in 94% of cases participants report that, while dreaming, their thoughts relate to the hallucinatory environment, the current findings argue against the widespread notion that "the sleeping brain can, in fact, either generate its own perceptions or it can think about them, but it cannot do both at the same time." (Scarone et al., 2007).

In this regard, our findings are consistent with early examinations of dreaming cognition by Aristotle (350 BC) and Descartes (1637) in that the relationship between perceptions and internal thoughts are described as essentially similar in waking and dreaming, i.e., we reflect on what we perceive whether the environment is hallucinatory or "real." Here we clarify how this relationship is modulated in REM and S2 sleep by demonstrating that in dreaming, like in the waking state, internal thoughts about the environment are logically sound while, unlike in the waking state, our ability to evaluate the novel nature of item-context relationships and the illogical aspects of that environment is deficient.

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Table 1. Overlap between regions implicated in logical thinking and regions hypoactive in REM sleep.

Phases of Deductive Reasoning	Brain regions involved [1]	Status in REM Sleep vs. Wake	Status in Stage 2 Sleep vs. Wake
Processing	Middle occipital gyrus L: BA 37 R: BA 37	No Change[2]	No Change[6]
	Inferior occipital gyrus L: BA 19 R: BA 19	No Change[2]	No Change[6]
	Inferior occipital	No Change[2]	No Change[6]
Integration	Medial prefrontal R: BA 10	No Change[2]	No Change[6]
	Cuneus R: 18	No Change[3,4,5]	No Change[6]
	Fusiform gyrus L: 37/20 R:19	No Change[3,4,5]	No Change[6]
	Anterior cingulate (R & L) BA 32	Increase [3,4,5]	**Decrease (L)**
	Parahippocampal gyrus (L) BA 36	Increase [4,5]	**Decrease (L)**
	Cerebellum	No Change[3,4]	No Change[6]
Validation	Middle frontal gyrus L: BA 6/9 R: BA 6	**Decrease[2]**	**Decrease[6]**
	Precentral gyrus L: BA 6	**Decrease[2]**	No Change
	Medial prefrontal BA 32	No Change[2]	**Decrease[6]**
	Inferior parietal lobule BA 40	**Decrease[2]**	**Decrease (R)**
	Precuneus	**Decrease[3]**	**Decrease**

[1] Fangmeier et al., 2006; [2] Maquet et al., 2005; [3] Maquet et al., 1996; [4] Nofzinger et al., 1996; [5] Braun et al., 1997; [6] Kaufmann et al., 2006

Table 2. Distributions of ratings for bizarreness, awareness of bizarreness and logical rigor.

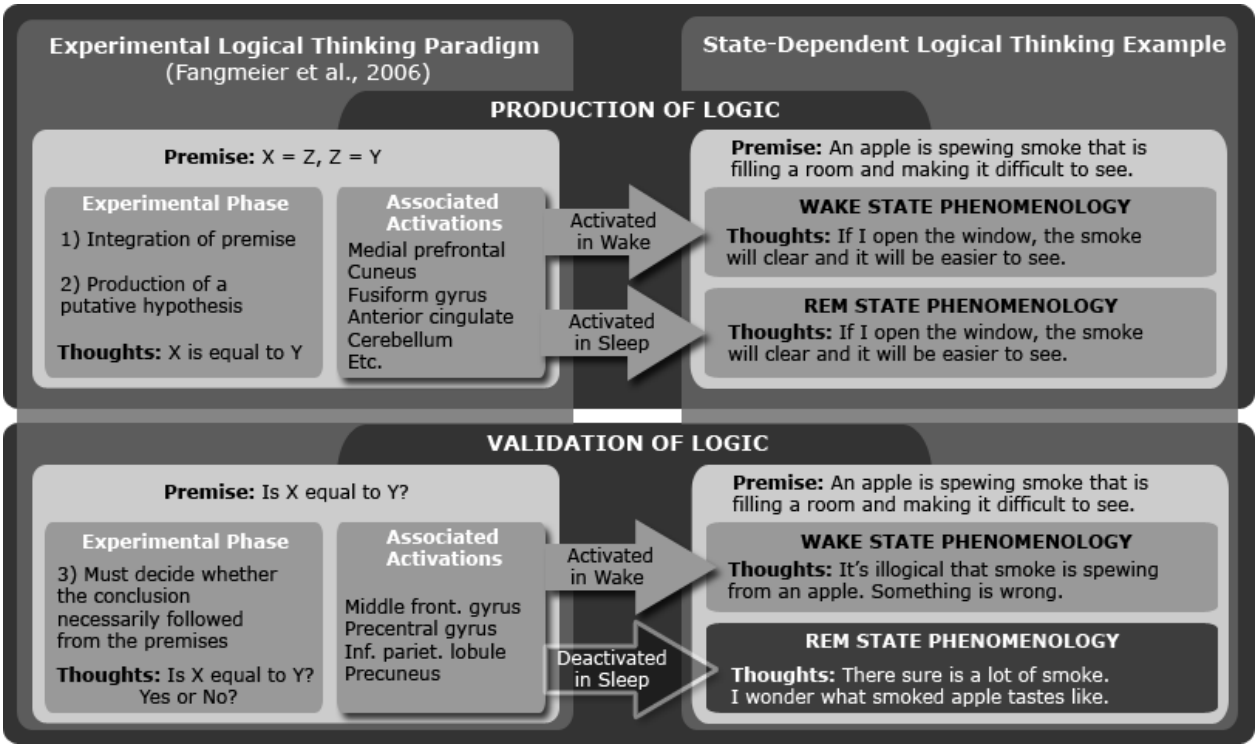
	Degree of Bizarreness		**Awareness of Bizarreness**		**Logical rigor**	
Rating	REM[a]	Stage 2	REM	Stage 2	REM	Stage 2
1	12	9	13	5	0	0
2	2	2	0	2	0	0
3	9	1	5	0	0	0
4	1	0	2	0	0	0
5	8	2	2	1	1	0
6	2	1	2	0	0	1
7	3	1	0	0	3	0
8	0	0	0	1	3	4
9	1	2	2	0	6	2
Mean (SD)	3.94 (1.61)	3.14 (2.53)	2.46 (1.72)	3.46 (3.22)	8.42 (1.20)	8.06 (0.94)

[a]*Each instance represents a single dream report.*

Table 3. Examples of bizarreness as a violation of context and/or logic.

Example of violation of context	Someone is selling cars at a student cafe. *Participant 3; late night Stage 2.*
Example of violation of logic	Participant ends up in the same bar, no matter what direction is taken. *Participant 5; early night REM.*
Example of a violation of logic and context	Participant is at the neighbour's house in the middle of the night. The walls are made of cardboard. *Participant 6; early night REM.*

Figure 1. Dissociation of the production and the validation of logic and their status in REM and S2 sleep cognition.



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CHAPTER V

General discussion

Discussion of articles I and II

The objective of the study was to examine the effect of REM deprivation and dreaming on the consolidation of the "what", "when", "where" and autonoetic components of episodic memory. Contrary to our expectations, we found limited evidence of a link between episodic memory and REM sleep and of an association between episodic memory and dreaming. Factual/perceptual and temporal features of episodic memory, as well as autonoetic awareness, were not associated with dreaming or with REM sleep as hypothesized. Rather, the results of articles I and II suggest that different aspects of episodic memories are associated with different stages of sleep, echoing previous descriptions of complex relationships between tasks and sleep phenomena (Fogel et al., 2007).

SWS was found to be associated with the consolidation of factual/perceptual features of the task. Similarly, SWS was associated with improved memory for spatial elements of the task in the low emotion but not the high emotion condition. SWS may be conducive to the consolidation of memories by virtue of the neocortical-hippocampal (NC-HC) communication co-occurring with sharp wave ripples known to be associated with plasticity at this time. In a prevailing view of declarative memory, the hippocampal complex processes the spatiotemporal context of memory while its perceptual features are dealt with in neocortical areas. Whether the memory trace migrates to neocortical areas over time (Squire, 1986, Squire et al., 2004), or remains dependent on the hippocampus (Nadel and Moscovitch, 1997) is a matter of current debate, but both views share the idea that spatial features of a memory are largely (at least initially) hippocampus dependent, while perceptual features are dependent on HC-NC interactions. During SWS, replay of pre-sleep activity in the HC (Wilson & McNaughton, 1994; Lee & Wilson, 2002; Ji & Wilson, 2007) is synchronized with replay in NC areas such as the prefrontal (Peyrache et al., 2009), parietal (Qin, et al., 1997) and visual cortices (Ji & Wilson, 2007). This HC-NC replay is synchronized to plasticity-inducing (Bramham & Srebro, 1989) sharp wave ripples, which have been associated with learning (Ego-Stengel & Wilson, 2009; Girardeau, 2009; Ramadan, 2009). In addition, the slow EEG oscillations characterizing SWS may have a direct link with consolidation of declarative memories, as suggested by the finding that

modulating the amount and amplitude of slow wave oscillations with trans-cranial magnetic stimulation (Marshall et al., 2004) or auditory stimulation (Landsness et al., 2005) produces an increase or a decrease in the recall of declarative materials, respectively.

The role of SWS in declarative memory processing is also supported by numerous studies finding an association between SWS and the learning of spatial tasks (Plihal & Born, 1999; Peigneux et al.,2004; Rasch et al., 2007; Rudoy, et al., 2009) and word lists (Fowler et al., 1973; Plihal & Born, 1999; Gais et al, 2002; Gais & Born, 2004). Together, these findings suggest that SWS is ideally suited for the strengthening of declarative memories and integrating them within neocortical areas. If the present findings of an association between SWS and the consolidation of factual and perceptual features of episodic memory (Article I) and low emotion spatial memory (Article II) fit well within the current literature, the findings for REM sleep require a more nuanced argument. REM sleep was not found to be associated with factual/perceptual and temporal features of episodic memory. Rather, %REM was found to be correlated with spatial memory for high emotion but not low emotion locations.

While hippocampal reactivation of pre-sleep exploratory behavior has been found to take place in REM sleep (Louie & Wilson, 2001), unlike in SWS, this replay does not involve synchronized NC replay and suggests that the transfer of memories from HC to NC does not occur at this time. With the exception of a few studies (e.g., Rauchs et al., 2004) and of studies utilizing emotional items, REM sleep is not associated with the consolidation of declarative memory in humans. This may explain why REM sleep was not associated with factual/perceptual and temporal aspects of episodic memory in the present study. However, REM sleep is characterized by co-activation of the hippocampus and amygdala, which are particularly synchronized at the theta band frequencies (Pare & Gaudreau, 1996; Hegde et al., 2010). Because emotional memory formation in the waking state involves a similar co-activation (Hamann, et al., 1999; Canli., 2000; Dolcos et al., 2004) and theta-band synchronization (Seidenbecher, et al., 2003; Pape et al., 2005) of the hippocampus and amygdala, similar emotional declarative memory processing may occur in the two states. In the waking state, theta frequency stimulation characterizes synaptic plasticity in both the hippocampus (Larson & Lynch, 1986; Staubli & Lynch, 1987) and amygdala (Heinbockel & Pape, 2000;

Pollandt et al., 2003). During REM sleep, theta synchronization between the hippocampus and amygdala is even further enhanced during episodes of increased PGO-wave density (Karashima et al., 2010), which is in turn associated with increased plasticity–related gene expression in the hippocampus and amygdala (Datta, Li & Auerbach, 2008). These findings are consistent with the notion that REM sleep is neurobiologically suited to process emotional memories.

However, it is less clear why emotion and REMD only influenced spatial aspects of the episodic memory task. Perhaps features that critically require processing from both the amygdala and the hippocampus, such as the spatial features of emotional memories, are highly sensitive to REM deprivation. These concerns notwithstanding, we have demonstrated, for the first time, that whether a task (in this case, a spatial task) is associated with SWS or REM sleep depends on its emotional value.

Dreaming of the VR task was associated with improved performance in spatial aspects of the episodic recall task, thus supporting the recent finding that dreaming of a spatial task at sleep onset and stage 2 sleep predicts sleep dependent learning on this task (Wamsley et al., 2010). Here we demonstrate that this may be specific to spatial learning, although it is not clear why this is the case. Nevertheless, spatial memory seems to be particular in that for this study it is associated with REM sleep, emotional memories, and dreaming. The notion that spatial aspects of episodic memories are central in scene construction (Hassabis & Maguire, 2007) may relate to this set of findings.

An informal analysis of dream reports indicated that isolated elements of the task were incorporated within dreaming. For example, one of the events of the negative task is a wild cat attacking a character. A participant dreamed of being chased through the jungle by a wild cat. In another example, the participant mentioned that the building she was in had some of the same features as the buildings in the neutral task. In all cases, incorporations related to select characteristics of the task (an item, character, structure, task objective). Moreover, these isolated elements were mixed with non-task related elements in the dream.

The tendency for REM sleep and dreaming to loosen associations between memory items may underlie the findings in the present study that, with the exception of spatial features of emotional episodic memory, REM sleep was not associated with the

consolidation of episodic memory and that dreaming was not generally associated with episodic memory consolidation. Previous research indicates that REM sleep is associated with increased performance in a creative performance task; it appears to prime associated networks and enable the integration of unassociated information (Cai et al., 2009). It is also associated with a bias towards weak, as opposed to strong, semantic associations (Stickgold et al., 1999). This suggests that REM sleep is involved in loosening or suppressing previous associations and even creating new ones. Phenomenological observations also suggest that dreaming is composed, in part, of fragments of episodic memory that are rearranged and result in bizarre combinations. Indeed, we observed that the VR-task was incorporated into dreaming in a fragmented manner, with isolated elements of the task being interwoven with other unrelated elements. REM sleep may not be suited for the consolidation of episodic memories, but instead be suited to the undoing of previous associations and the forging of new ones. This possibility was examined in article III (see below).

Autonoetic awareness during the episodic memory task was found to be associated with stage 2 during the last third of the night. This finding suggests that previous reports of an association between late night sleep and autonoetic awareness at recall (Rauchs et al., 2004) may not be related to REM sleep as the authors propose, but rather to late night stage 2 sleep. Although late night stage 2 sleep is characterized by increased spindle activity (Jankel & Niedermeyer, 1985; Guazzelli et al., 1986), which in turn is associated with plasticity, it is not clear how this plasticity may translates into an improvement in the ability to view spatial information with “the mind's eye.” Nevertheless, this result suggests that REMD is a useful method for gauging the relative contributions of different sleep stages. This may give REMD an advantage over the late night-early night method used in many studies; the latter authors assume, incorrectly, that late night sleep selectively favours REM sleep. But, in fact, stage 2 sleep is also abundant at this time. As demonstrated by the current results where a strong association between Stage 2 in the final third of the night and autonoetic awareness was found, the time of night may be a critical factor in the relationship between a sleep stage and the processing of a task or task element.

Overall, the results of article II are consistent with predictions based on phylogenetic parallels between the evolution of memory systems and sleep stages, as described below.

Phylogenetic relationships between sleep and memory

Research suggests that fish species such as salmonid (Nordgreen et al., 2010) and teleosts (Portavella et al. 2003; Nilsson et al. 2008) form declarative representations suggestive of semantic-like 'knowing what' knowledge about the relationship between food and light cues. Episodic-like memory, on the other hand, seems to be restricted to mammals and birds. Specifically, flexible knowledge of the 'what' 'where' and 'when' of events have been found in scrub-jays (Clayton & Dickinson, 2003), magpies (Zinkivskay at al., 2009), rats (Babb & Crystal, 2006) and great apes (Martin-Ordas et al., 2010). However, these experiments measured "episodic-like memory" because they could not assess phenomenological features of episodic memory. It has been argued that autonetic awareness is uniquely human (Tulving, 2002; Suddendorf & Corballis, 2007) and has played a large and unique role in hominid evolution (Suddendorf, 2006; Suddendorf & Corballis 2009).

To the extent that SWS and REM sleep are implicated in memory processing, it might be expected that animal species displaying SWS and REM sleep possess types of memory that are absent in species lacking SWS or REM sleep. As described earlier, only birds and mammals are endowed with both episodic-like memory and SWS and REM sleep. In contrast, the autonoetic awareness component of episodic memory has only been demonstrated in humans, who may be also unique (as primates) in expressing stage 2 sleep.

Indeed, stage 2 sleep may be unique to primates in that it occupies a very large proportion (approximately half) of each sleep session. In rats and cats an intermediate stage characterized by high-amplitude anterior cortex spindles and low-frequency hippocampal theta rhythm precedes and sometimes follows REM sleep (Gottesmann, 1996). However, such intermediate sleep only lasts 1-5 seconds in rats (1-3 seconds in cats), is present before REM sleep 75% of the time (27% in cats), and is only present after REM sleep 15% of the time (4% in cats). Intermediate sleep is therefore a very brief transitory period quite different from the extended episodes of Stage 2 sleep in

primates. To my knowledge the question of whether extended Stage 2 sleep is unique to primates has not been directly addressed, although Gottesmann's (1996) findings demonstrating its absence in rats and cats, but its presence in monkeys (e.g., Reite et al., 1976) suggests that it may well be.

Together, these observations support the suggestion that the evolution of SWS and REM sleep in birds and mammals co-occurred with the evolution of episodic memory and, therefore, that the two are functionally related. Similarly, the evolution of stage 2 sleep in humans may have co-occurred with the evolution of the autonoetic awareness component of episodic memory. It is therefore predicted that SWS and REM sleep are involved in the 'what', 'when' and 'where' elements of episodic memory while Stage 2 is involved in the autonoetic component of episodic memory. The present findings of associations between SWS and the "what" aspects of episodic memory, and of stage 2 and its autonoetic component, are consistent with these predictions and support the notion of functional relationships between the evolution of specialized sleep states and that of complex declerative memory.

Discussion of article III

The objective of the study was to evaluate whether dreaming involves hippocampally-mediated, declarative memory processes. The study employed a highly trained participant to provide detailed descriptions of dreaming and its memory sources. We applied a method that produces multiple, short, well-remembered dreams during a period of NREM1 in which features of REM sleep (e.g., theta activity) are found (NREM1Φ).

Awakenings gave rise to reports of vivid dreaming depicting items that were well integrated within a three dimensional environment. These qualities of imagery, i.e., "scene construction", are indicative of hippocampal involvement (Hassabis & Maguire, 2007) and consistent with the claim that the hippocampus is involved in NREM1Φ dreaming at this time.

The results also suggest that during dreaming new associations are forged between distally related items and that multiple memory sources for a single dream appear to be selected on the basis of both semantic proximity and temporal distance. It may be that the novel co-occurrence of previously unrelated items within the spatial-

temporal context of the dream reflects a mechanism by which offline integrative encoding occurs, a hippocampally-mediated process by which items from separate events are merged into a shared mnemonic representation (Shohamy & Wagner, 2008).

While subjects usually do not remember their NREM1Φ dreams unless they are awakened at this time, here we demonstrate that they are nonetheless vividly perceived. NREM1Φ is characterized by the appearance of saccade-like slow eye movements (Porte, 2004) suggesting that attentional mechanisms may be active at this time. Furthermore this state is characterized by the disappearance of the N300 mismatch negativity, which suggests a switch from external to internal processing of stimuli (Nittono et al., 2001).

The common belief (e.g., Freud, 1900) that dreams draw upon and combine multiple memory sources to produce coherent, often creative, imagery may be particularly true for sleep onset dreaming. Numerous examples illustrate how individuals gain important insights into a creative problem from sleep onset dreaming. For instance, Edison and Dali, known for their creative use of sleep onset imagery, were highly practiced at recalling sleep onset imagery, each having developed a technique for arousing themselves from such imagery and applying it to problem-solving (Dali, 1963; Mavromatis, 1987). Such anecdotes illustrate that sleep onset imagery may be usefully applied to the question of the memory sources of dreaming. Not only does it give access to fragments of episodic memories (e.g., Kekule's images of 'floating atoms') but it is in many respects a learnable skill.

A curious property of dreams relates to the fact that loosely related associations are bound together into coherent representations that are bizarre, yet go unnoticed while the dream is unfolding. It is unclear whether this feature of dreaming is indicative of a generalized diminishment of cognitive ability or rather a selective reduction of a particular aspect of thinking. Moreover, it is unclear whether dream bizarreness reflects novel associations between memory items and contexts. Article 4 addresses these questions by examining if, during dreaming, the ability to appreciate bizarreness is selectively diminished. The study also examines the question of whether dream bizarreness is the result of novel associations.

Discussion of article 4

It is widely believed that during dreaming we do not realize that we are dreaming. Is our dream self, as Allen Rechtschaffen (1978) claimed, “isolated and single minded”? The fact that during dreaming we usually do not realize that bizarre events and objects are bizarre has led to the conclusion (e.g., Hobson, 2004) that the dreamer is unable to think logically. Such a pronounced deficit would appear to contradict the notion of cognitive equivalency between waking and dreaming states (Kahan and LaBerge, 1994).

However, apart from bizarre features, dreamers may be deceived into thinking a dream is reality because the perceptual qualities of the dreaming environment appear extremely real. Indeed, the highly efficient reality mimesis of perceptions during dreaming (Nielsen and Stenstrom, 2005; Renvonsuo, 2000) may render it impossible to distinguish dreaming from waking on the basis of perceptual qualities alone. As suggested by studies of lucid dreaming (LaBerge, 1985), dreamers can only become aware that they are in fact dreaming in reaction to inconsistencies among the elements of the dream, but not simply on the basis of the quality of the apparent percepts in the dream. Thus, what is particular about critical reasoning in sleep may be that bizarre elements within the dream environment cannot be questioned as long as they are embedded in a perceptually authentic medium.

This hypothesis is tested in article 4 by waking participants from REM sleep and directly asking them if, during dreaming, their thoughts were logical and whether they could appreciate the bizarre nature of their dreams. In addition, we examined if dream bizarreness is the result of novel associations between memory items as previously suggested.

The results suggest that participants do not appreciate bizarre features of the dream environment, but rather report thinking logically about them. In addition, the results indicate that dreamed bizarreness seems to involve elements that are out of context, that is, items that are associated with novel contexts. This adds to our previous observation (article III) that dream bizarreness often results from novel associations between items. Together, the findings suggest that bizarreness in dreaming is the result of novel associations between items and between items and their contexts. This is consistent with previous findings indicating that REM sleep is conducive to the

production of weak, as opposed to strong, associations among memory elements (Stickgold et al., 1999).

If the logical rigor of thinking is maintained during dreaming, why is the ability to detect dream bizarreness absent or diminished? One explanation is that while bizarreness is inherent to the production of dreaming, the successful detection of bizarreness may induce a form of self-reflection that prompts awakening. Indeed, lucid dreaming (the realization that one is dreaming while dreaming) is often achieved when one appreciates that something is bizarre in the dreamed environment (LaBerge, 1985). Lucid dreaming is known to produce involuntary awakenings (LaBerge, 1985) and is associated with high alpha activity (Ogilvie et al., 1982; Tyson et al., 1984), a marker of arousal from sleep (Rechtschaffen & Kales, 1968). It is thus possible that diminished awareness of bizarreness may protect sleep from the arousing effect of knowing that one is dreaming. Also, upon reaching a lucid dreaming state the individual sometimes changes the content of the dream (Kahan & LaBerge, 1994), which may be problematic if the content of the dream is of functional importance (c.f., Freud, 1900; Revonsuo, 2000). Or, a function of dreaming may depend upon the individual truly believing that their current dream situation is reality. For example, believing that the dreamed environment is real is thought to ensure that engagement and emotional responses are maximised (Nielsen & Levin, 2008).

Finally, it is suggested that the diminished ability to detect bizarreness may relate to altered functioning of the hippocampus. The role of the hippocampus in novelty detection is dependent upon communication between CA1 and DG/CA3 areas (Hasselmo and Schnell, 1994; Lisman & Otmakhova, 2001). Diminished gamma and theta coherence between CA1 and DG-CA3 networks during REM sleep (Montgomery et al., 2008) suggests that the ability of hippocampus to function as an item-item/item-context novelty detector may be diminished at this time. This suggests that altered hippocampal functioning in sleep may not only give rise to bizarreness by binding loosely associated memory items, but may also underlie the diminished ability to appreciate the resulting bizarreness.

Study limitations

An important limitation of articles I and II lies in the fact that the VR task and related memory questionnaire are novel and have not been validated. Second, there was no direct measure of state or trait emotional reactivity. Considering the importance of emotions in article II, the lack of an emotional measure is a weakness of this study. In addition, because of the study's emphasis on REM sleep an adaptation laboratory night would have been preferable to avoid the possible confounding effects of the first night effect (Lorenzo & Barbanoj, 2002). The study would have also benefited from a greater number of male participants, although the two sexes were equally distributed across the two groups.

A major drawback of article III is the use of a single participant. Conclusions drawn from the study are thus tentative and require confirmation. A second weakness of this study was that theta activity at sleep onset was (by necessity) visually detected but not later confirmed by off-line spectral analysis. A final weakness is that this participant's training procedure could have been more systematic documented. Notwithstanding these weaknesses, however, the successful use of a single trained individual to lay bare important features memory processing in dreams constitutes an important proof of principal and paves the way for future group-level studies.

A limit of article IV is that only a single judge evaluated whether dream bizarreness was the result of a violation of logic or a violation of context. A second limit is that, as in articles I and II, participants were predominantly female and thus the findings may not generalize to males.

General summary & discussion

In summary, our findings and the evidence reviewed here suggest that SWS neurophysiology is ideally suited for solidifying existing memory associations while REM neurophysiology may be better suited for loosening existing memory associations and creating new ones. Indeed, in article I the consolidation of factual/perceptual elements of episodic memory was associated with SWS sleep, while REM sleep dreams incorporated isolated elements of the VR task that were associated with unrelated imagery. In article III, we found evidence that memory elements composing dreams reflect distal temporal relationships, consistent with the notion that dreaming is involved in loosening existing associations and creating new associations between memory

items. It is suggested that dreaming may enable items from temporally distal memories to be associated by virtue of their simultaneous appearance within a novel spatial-temporal context afforded by the dream. Article 4 also provides evidence that dream bizarreness often relates to novel and unusual associations between an item and its context and reveals that REM sleep cognition is deficient in a manner such that bizarreness is not questioned. Maintenance of the ability to think logically in the dream suggests that this deficiency is selective. This cognitive diminishment may allow the dreamer to believe that they are perceiving reality and to ensure that they are engaged in and attentive toward bizarre item-item and item-context combinations provided by the dream.

Why does dreaming have such a persuasive tendency to make use of novel and bizarre associations? Some authors have suggested the lack of hippocampal involvement in dreaming is responsible for bizarre dream features (Stickgold et al., 2000; Stickgold et al., 2001; Payne and Nadel, 2004). However, the observation that scenes are constructed during dreaming in article III suggests that the hippocampus is active during dreaming. This leads to the notion that novel and bizarre associations between items, and between items and contexts in dreaming are not a sign of a deficient binding (Revonsuo & Tarkko, 2002) or deficient hippocampal function (Stickgold et al., 2000; Stickgold et al, 2001; Payne and Nadel, 2004) but rather suggests that this feature may serve a function.

Given that hippocampal plasticity is largely experience dependent (Butz et al., 2009; Feldman, 2009; Holtmaat and Svoboda, 2009) and modulated by attention (Muzzio et al, 2009, Muzzio, Levita et al, 2009), it may be that the *subjective* experience of dreaming plays a causal role in whatever memory functions occur during REM sleep. This is because subjective experience provides the hippocampus with an attention-engaging experience during which items of semantic value taken from remote memories are presented together in close proximity within the same spatiotemporal context. Although this experience may not lead to the formation of an episodic memory (unless the person is awakened at this time), synaptic weights in hippocampal networks may nonetheless undergo modification in a manner similar to the effect of waking experience on hippocampal plasticity; namely, strengthening associations between the

neural representations of the once distal items by virtue of the temporal and spatial proximity afforded by novel item-context configurations during dreaming.

The notion that the subjective experience of dreaming could enable plasticity echoes David Hartley's (1749) suggestion that dreaming may alter associations of the mind. Today modern neuroscience considers neural ensembles (engrams) as the basis of memory, synaptic plasticity as the basis for the formation and modulation of memory and experience as the principal driver of synaptic plasticity. It would therefore be highly significant if it were demonstrated that the experience of REM sleep dreaming modulates cerebral plasticity. In particular, it would suggest a vital function for REM sleep and REM sleep dreaming. The following section examines this possibility.

An exploratory review of how dreaming may influence brain plasticity

Research presented in this dissertation is consistent with the possibility that, in dreams, memory elements are manipulated in a manner that allows for the creation of novel, bizarre, item-item and item-context associations. Further, these novel associations may be implicated in processes of long-term consolidation. This exploratory review examines these possibilities, i.e., the notion that the phenomenological aspects of dreaming described in articles I-IV have long-term consequences on the plasticity of neural networks. First, the elements required for synaptic plasticity are reviewed. Second, whether these elements are present in REM sleep and REM sleep dreaming are examined. Finally, possible consequences of dreaming-induced plasticity on memory systems are addressed.

Brain plasticity

The cellular basis of memory concerns changes in synaptic strength between neurons (Bliss & Collingridge, 1993; Bear, 1996). Through synaptic plasticity the mature cerebral cortex can modulate its connectivity as a result of experience. Sensory experiences can alter the connection strengths of neurons (synaptic plasticity) and change the structure of existing networks (structural plasticity) via the formation and elimination of synapses (Holtmaat & Svobaoda, 2009)—a process believed to underlie long-term memory formation (Bailey & Kandel, 1993). A major mechanism of long-term synaptic plasticity is long term potentiation (LTP), defined as a long-lasting

potentiation of the excitatory post-synaptic potential of fields of two neurons that fire in spatial and temporal proximity. This potentiation results in the modulation of synaptic strength between two neurons. LTP is found, notably, in the hippocampus, amygdala and prefrontal cortex, and it has been suggested that all excitatory synapses in mammalian brain may undergo LTP (Malenka & Bear, 2004). The processes of LTP can be divided into early and late effects. Early LTP is a calcium-mediated, NMDA-dependent process that is accomplished without protein synthesis. Late LTP involves changes in gene expression and the synthesis of proteins. Resulting proteins are believed to contribute to an increased number of dendritic spines and increases in the number of synaptic vesicles in both the pre and post-synaptic cell (Lynch, 2004). In addition, late LTP is believed to be involved in the production of new synapses (Toni et al. 1999; Antonova et al., 2009). Axonal buttons grow, are eliminated or are modified in response to experience (Tashiro et al., 2003; De Paola et al., 2003). Axon sprouting is observed as a result of environmental enrichment (Galimberti 2006) or spatial learning (Ramirez-Amaya 2001; Holahan et al., 2006). In sum, experiences rewire the brain and these modifications of neural networks are thought to reflect learning and memory.

Long-term depression (LTD) has also been identified as a mechanism of cerebral plasticity. Where LTP is involved in encoding novelty, LTD may encode the lack of new features (Poe et al., 2000; Romcy-Pereira et al., 2009).

Plasticity in REM sleep

Several lines of research suggest that neural plasticity can occur during REM sleep. First, LTP in the dentate gyrus is readily induced in wake and REM sleep but not SWS (Bramham & Srebro, 1989). LTP following avoidance training was also induced in REM sleep but not wake (Winson & Abzug, 1977; 1978). Recently, Ravassard et al., (2009) found evidence that REM sleep is associated with late, and not early LTP in the dorsal hippocampus. Neuromodulatory aspects of REM sleep—increased levels of acetylcholine in particular—may also benefit plasticity as this neurotransmitter is associated with increased LTP in the hippocampus (Aguiar et al., 2008). Acetylcholine is well known to enhance hippocampal plasticity (Jerusalinsky et al., 1997; Power et al., 2003; Hasselmo, 2006) and has been recently shown to act synergistically with theta oscillations to promote neural plasticity (Zhang et al., 2010). While norepinephrine and

serotonin are greatly diminished in REM sleep, the brain is flooded with acetylcholine— and characterized by dominant theta oscillations— during this stage of sleep.

Second, REM sleep is characterized by plasticity-related genetic expression. Specifically, an important experience- and plasticity-related gene, ziff-268, is expressed in REM sleep but not SWS (Riberio et al., 1999, 2007). Ziff-268 is reliably induced by LTP (Cole et al., 1989) and is strongly associated with dendritic changes resulting from exposure to novel environments (Wallace et al., 1995). Functional rewiring may occur as a result of dendritic growth (Holtmaat et al., 2009). In addition, PGO waves characterizing REM sleep are associated with increased plasticity–related gene expression in the hippocampus and amygdala (Datta, et al., 2008).

In sum, REM sleep is characterized by tonic (high levels of acetylcholine, theta oscillations), phasic (PGO waves) and genetic (Ziff-268 expression) phenomena strongly associated with plasticity. More specifically, REM sleep is associated with LTP, a process related to the encoding of novel environments, and in particular late LTP (Ravassard et al., 2009) that is associated with structural plasticity (Holtmaat & Svoboda, 2009). It is therefore likely that structural plasticity associated with novelty occurs during REM sleep.

It is currently debated whether SWS is a state conducive to plasticity, with some authors arguing for (Diekelmann & Born, 2010) and some against (Ribiero 2007) this notion. One the one hand, spindles characterizing NREM sleep may be associated with plasticity (Steriade, 1999, Sejnowski & Destexhe, 2000) and are involved in human memory (Schabus et al., 2008); also, SWS is characterized by activity within regions closely associated with plasticity (e.g., the hippocampus and prefrontal cortex; Dang Vu et al., 2008). On the other hand, phenomena known to be associated with plasticity, i.e., ziff-268 expression, PGO waves, theta and acetylcholine, are abundant in REM and absent from SWS sleep. That SWS plays a minimal role in synaptic plasticity is also consistent with the notion that synaptic downscaling may occur during this time (Tononi & Cirelli, 2003). Overall, when comparing SWS and REM sleep, only the latter seems to be characterized by an abundance of the neurophysiological features known to induce plasticity.

Synaptic plasticity & and experience

Several lines of evidence converge on the notion that the novelty of experience is an important factor in its ability to induce neural plasticity. In a review of PET studies examining memory, Tulving et al (1996) proposed that the probability of long-term storage of information varies in direct proportion to the novelty of this information. Exposure to new environments triggers LTP in multiple areas of the hippocampus (Manahan-Vaughan & Braunewell, 1999). In addition, exposure to novel environments lowers the threshold for LTP induction in CA1 (Li et al., 2003). Novel spatial exploration is also associated with theta band activity, which is argued to be critical for encoding information in hippocampal cell ensembles (Buzsáki et al., 2002). Indeed, the modulation of hippocampal synaptic weights is critically dependent on theta activity (Kamondi et al., 1998). Also, recent studies have demonstrated that hippocampal plasticity is facilitated by attention (Muzzio, Kentros et al, 2009, Muzzio, Levita et al, 2009), motivational states and emotions (Conway, 2005). If these plasticity-enhancing factors—novelty, attention, motivation and emotion—are also present during dreaming, then there would be ample reason to believe that dreaming, too, enhances memory. The following section examines if these characteristics are typically present in REM dreaming.

Elements of dreaming associated with synaptic plasticity

Novelty

Because dreaming appears to combine isolated memory features of all kinds in a constant flow (Nielsen & Stenstrom, 2005), the perception of novel visual, auditory and motivational elements is typical. The ubiquity of character imagery in dreams illustrates this point. REM sleep mentation features an average of 3.9 characters per report, 48% of which are unknown to the individual (Kahn et al., 2002). Characters are thus a constant source of novelty in dreams. The results of studies presented here support the notion that novelty characterizes dreaming. In Article III only 1 of 31 dreams consisted of a replay of a previous event while all other dreams were characterized by novel memory item associations. Similarly in Article 4 we found several instances of novel and bizarre relationships between items and contexts. Dreams are therefore a source of constant and sometimes bizarre novelty and, in this sense, dreams provide new

environments that are explored (see later section on motivational states in dreaming). Consistent with this notion is prominent theta activity during REM sleep and during the REM-like Hori Stage 5 of NREM1 sleep where a majority of dreams occurred in novel environments in which the dreamer was engaged in (virtual) motor activity.

Attention

Morrison (1983) has explained the consistent presence of PGO activity during REM sleep as a type of ongoing orienting response triggered by the constantly novel contents of dream imagery. In a recent fMRI study of sleep, Hong and al., (2009) provide supportive evidence that the rapid eye movements of REM sleep are visually-targeted saccades and share underlying brain systems and mechanisms with waking eye movements. These findings are taken to suggest that attentional systems are active in REM sleep and reflect the visual exploration of dream imagery. While there is disagreement about whether all eye movements reflect a type of visual 'scanning' of the dream environment (Ogawa, et al., 2002), it is likely that at least some eye movements do (Herman, 1984).

Motivational states & emotions

Motivational factors are central to psychodynamic theories of dreaming. They have recently been empirically studied by Smith et al. (2004) who found that motivational content was more frequent in REM than in Stage 2 sleep mentation. Emotions are also present in most dreams (e.g., Foulkes et al., 1988) and central to dream formation (Freud, 1900; Hobson et al., 2000). Most emotions found in dreams are judged by subjects to be appropriate to the dreamed situations had these situations occurred during wakefulness (Foulkes, 1988).

The qualia of dreaming

Experience-driven plasticity may depend upon perceptual rather than imaginal experiences. For example, although imagery may activate the primary visual cortex or V1 (Kosslyn & Thompson, 2003), there is no indication that this cortical activity can induce plasticity. Consequently, it might be argued that dreaming cannot induce

plasticity because it does not possess the same sensory quality (or *qualia*) as waking perception. Qualia here refers to the phenomenological properties of sensory experiences (see Hogart, 1984).

However, in the following section we present evidence that dreaming may indeed be of the same qualia as waking perception and that dreaming may thus impact neural networks even if they cannot be recalled.

Is the neurophysiology of REM sleep sufficient to allow for wake-like perception?

Perception identical to waking state qualia can occur in the absence of external simulation. For example, hallucinations in otherwise healthy individuals, such as occur in Charles Bonnet syndrome, are reported to possess the same qualia as normal perception (ffytche, 2009). Considering the wide-ranging neural modulations accompanying REM sleep, the question of whether wake-like perception is possible in REM sleep would benefit from an examination of whether neural processes underlying wake-perception are available during REM sleep.

The ventral visual pathway, consisting of regions of the occipital and temporal lobes and the hippocampus system, is critical to conscious vision (Vogels & Orban, 1996). Brain imaging studies indicate that these areas are active in REM sleep, apart from a distinct pattern of activation in the occipital cortex. During REM sleep, there is activation within extrastriate areas but not in area V1 (Braun et al., 1997, Maquet et al., 2006). However, a recent study examining neural activation during phasic REM found increased activation in V1 during this time. This suggest that the neurophysiological characteristics of phasic REM in particular may support wake-like visual processes.

Several studies have linked gamma range activity (30-150 Hz) to conscious visual perception (e.g., Engel & Singer, 2001). For example, consciously perceived stimuli are associated with increased mid-frequency gamma-band activity over the contralateral visual cortex whether these stimuli are attended to or not (Wyart & Tallon-Baudry, 2008). If wake-like conscious perception occurs during REM sleep, then gamma activity would be expected during this state. Indeed, cortical gamma rhythm has been found during REM sleep (Llinas & Ribary, 1993). However, REM sleep is characterized by the absence of gamma rhythm reset (Llinas & Ribary, 1993) suggesting a diminution of cortical connectivity. REM sleep gamma activity is also

distinct from wake by the uncoupling of gamma rhythms between perceptual and frontal areas (Perez-Garci et al., 2001) and suppression of gamma rhythm coherence between the hippocampus and the cortex (Cantero et al., 2004). Despite these differences, however, a study employing a passive oddball procedure suggests that the gamma response during sleep is similar to sensory/perceptual processing in wakefulness (Karakas et al., 2006).

In sum, dreaming may consist of sensations that are of the same qualia as in waking state perception. This may be especially true for dreams occurring during phasic REM as the primary visual cortex is activated at this time. That dreams are remembered as perceptually diminished experiences when compared to waking state perceptual experiences may relate to the fact that dreaming occurs in a vastly different context and a neurophysiologically distinct brain state.

Functional aspects of dreaming

An average of 2 hours per day is spent in REM sleep and approximately 80% of awakenings from REM sleep provide reports of dreaming (Nielsen, 2000). If dreaming impacts neural networks in a manner similar to waking experiences, then what does a lifetime of dreaming do to the connectivity of the brain?

Waking experience alter neural networks in a manner that allows events to be visualized by means of imaginal scene construction. For example, an encounter with a cat will modulate neural representations related to the semantic/perceptual concept of cat that serves as the basis for the memory of the event. What does dreaming of this cat do to cat-related neural representations? As in waking experiences, it depends on what other items are present with that cat, as well as the context in which these items are found. Thus, the global effect of dreaming on neural networks may be understood by examining the manner in which memory items are used in dreaming. Specifically, during dreaming elements of waking experiences are mixed together in a manner that creates new item-item and item-context associations. By doing so it may loosen preexisting associations by presenting an item in the absence of a related item. In this sense, dreaming provides flexibility in mnemonic networks involved in scene construction by presenting item configurations that have not been provided by waking experience. This flexibility will be referred to as “scene construction flexibility” in

order to differentiate it from cognitive flexibility which does not necessarily relate to scene construction.

In the following, the adaptive and maladaptive aspects of scene construction will be examined in relation to dreaming.

Adaptive aspects of imaginal scene construction

Engaging in scene construction can be highly adaptive (see Szpunar 2009 for review). For example, the mental simulation of events can be beneficial for emotional regulation and problem solving (Taylor & Schneider, 1989). Scene construction may provide the means to anticipate obstacles and to generate hypothetical solutions (Hayes-Roth & Hayes-Roth, 1979; Taylor & Schnieder, 1989). Scene construction in the form of future projection may enhance goal achievement (Taylor et al., 1998; Pham & Taylor, 1999) as well as improve chances of implementing intentions (Golwitzer, 1993, 1996, 1999). In all such studies, the beneficial aspects of scene construction rely on novel configurations of memory items, i.e., participants were instructed to visualize scenes that were novel as opposed to episodic in nature.

Alternative associations between memory items may make memory networks more conducive towards forming new associations during scene construction of the problem solving kind. For example, new associations provided by dreams may serve to loosen the associations dream elements have with their original sources in waking experience. As William James (1890) suggested, creativity requires "(...) unheard of combination of elements (and) the subtlest associations (...)." (p. 456)

Maladaptive aspects of scene construction

In a similar fashion, some scene construction can have maladaptive consequences. Imagery may play an important role in many psychopathologies. Imagery of dirt and germs is associated with contamination fears in obsessive compulsive disorder (de Silva, 1986). Patients with social phobias imagine themselves in negative social situations while those with generalized anxiety disorder imagine themselves in feared situations (Hirsch & Holmes, 2007). Disturbed imagery is also associated with paranoid delusions in psychotic patients (Morrison et al., 2001). In posttraumatic stress disorder (PTSD), pathological imagery plays a central role. In this

case, traumatic events are replayed intrusively and in vivid perceptual detail both during waking, i.e., flashbacks, intrusive memories, and sleep, i.e., replay nightmares.

PTSD provides an extreme example of what may occur when an episodic memory fails to be processed in dreaming in a manner that provides scene construction flexibility. PTSD nightmares are abnormal in that they replay whole episodic memories, suggesting that processes involved in scene construction flexibility are dysfunctional at this time. Whereas only 1.6% of the dreams reported by healthy participants are episodic replays (Fosse et al., 2003), approximately half of nightmares reported by PTSD patients are considered "identical to flashbacks" (van der Kolk & Fisler, 1995) or "replicative dreams" (Schreuder et al., 2000). In PTSD, trauma memories are apparently not being successfully fragmented and re-associated with distal memory items or contexts during dreaming as should be the case.

Image rehearsal therapy for nightmares is highly effective in reducing all the symptoms of PTSD. This technique involves repeatedly visualizing a different ending to a nightmare, suggesting that the introduction of new item-context or item-item associations during waking can contribute to resolution of dysfunctional trauma memories. Image rehearsal therapy can therefore be understood as the manipulation of memory items in a dream-like manner (introductioning new item-context or item-item associations) in order to compensate for the lack of such processing during dreaming (i.e., replicative dreams).

Conclusion

REM sleep dreaming can be viewed as containing elements of waking perception as well as novel imaginal scene constructions. As suggested in Article III, dreaming may use hippocampally-mediated scene construction processes to give rise to novel virtual environments. However, unlike imaginal scene construction during wake, and in a manner similar to typical stimulus-driven perception of wake, these environments are taken to be reality. Selective cognitive deficits described in Article 4 allow the dreamer to remain immersed in the apparent reality of the virtual environment while still allowing wake-like cognition. As a result of a selective deficiency in appreciating the bizarreness of dream elements, the dreamer becomes immersed in, pays attention to, emotes and is motivated within the dream—despite its bizarre nature. In

turn, novelty, attention, emotion, and motivation are important modulators of synaptic plasticity.

Thus, not only is REM sleep a neurological state conductive to plasticity, but the principle qualities required to induce experience-related plasticity are consistently present during REM sleep dreaming. Novelty, a powerful driver of synaptic plasticity, is produced in the form of novel item-item and item-context juxtapositions. Dreaming qualia are akin in many respects to the types of waking perception that are necessary to impact neural networks. Features such as novelty and the exploration of environments may be even more characteristic of REM sleep dreaming than waking state experiences. Consequently, while the dreamed experience is not easily recalled it may significantly modulate synaptic weights of neural networks in a manner similar to, if not better than, waking experiences.

The manner in which dreaming impacts neural networks may depend on how it deploys memory items. As suggested by evidence presented in all 4 articles, dreams draw upon items from loosely related memories within novel contexts. Dreaming may therefore create novel associations between distally related memory items, and in doing so loosen existing associations between items. This process may enable scene construction flexibility. Adaptive use of scene construction may depend on the ability to make associations between items, and between items and contexts that are different from those previously experienced. Mnemonic flexibility provided by dreams thus may facilitate adaptive use of scene construction. In contrast, a lack of alternative associations between memory items may be maladaptive. Psychopathologies such as OCD, PTSD and schizophrenia all feature imagery that is intrusive, highly resistant to change, and which may exacerbate symptoms. In the case of PTSD, introducing new associations to the resistant, symptom-related imagery may help alleviate intrusions of that imagery as well as symptoms more generally. Scene construction is therefore adaptive if associations between memory items are flexible, but maladaptive when associations between salient memory items are rigid.

REM sleep may thus have a complementary role to SWS in the processing of episodic memory. SWS may be responsible for consolidating declarative memories while REM sleep provides links between memory items that differ from those found in

waking experience, a process that may enable scene construction to operate with optimum efficiency.

In closing, the ideas presented in this section are admittedly speculative. However, I hope to have made the case that the subjective experience of dreaming may have a causal role in memory processing, as opposed to the prevailing view which considers dreaming to be a consequence of memory processing (Wamsley et al., 2010), or to have no association with memory processing at all (Diekelmann and Born, 2010). Rather, the view espoused here is that dreaming is an elaborate orchestration of memory elements into novel, plasticity-inducing perceptual experiences. The latter establish new relationships between objects, people, places and events that are different from those previously encountered during wakefulness. Dreaming may therefore enhance the human capacity to imagine entirely new events and apply them to adaptive ends which is, as suggested by Jean-Paul Sartre (1940), a means of reaching "beyond reality."

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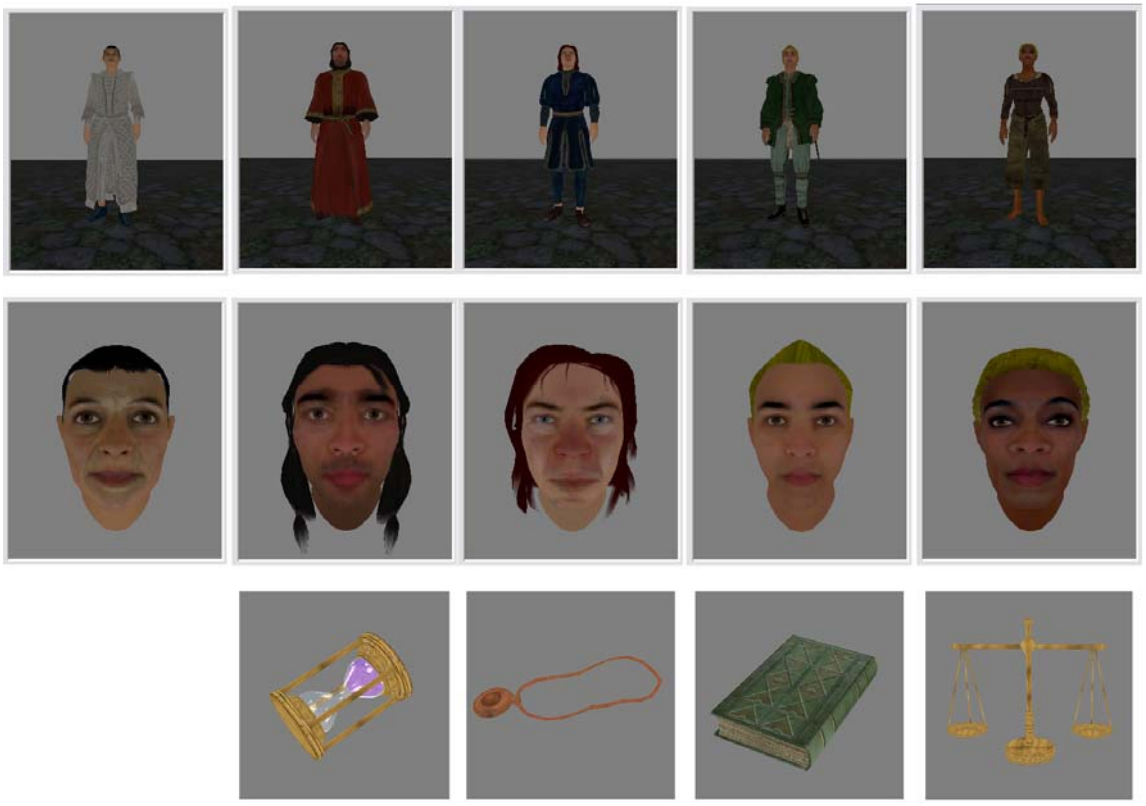
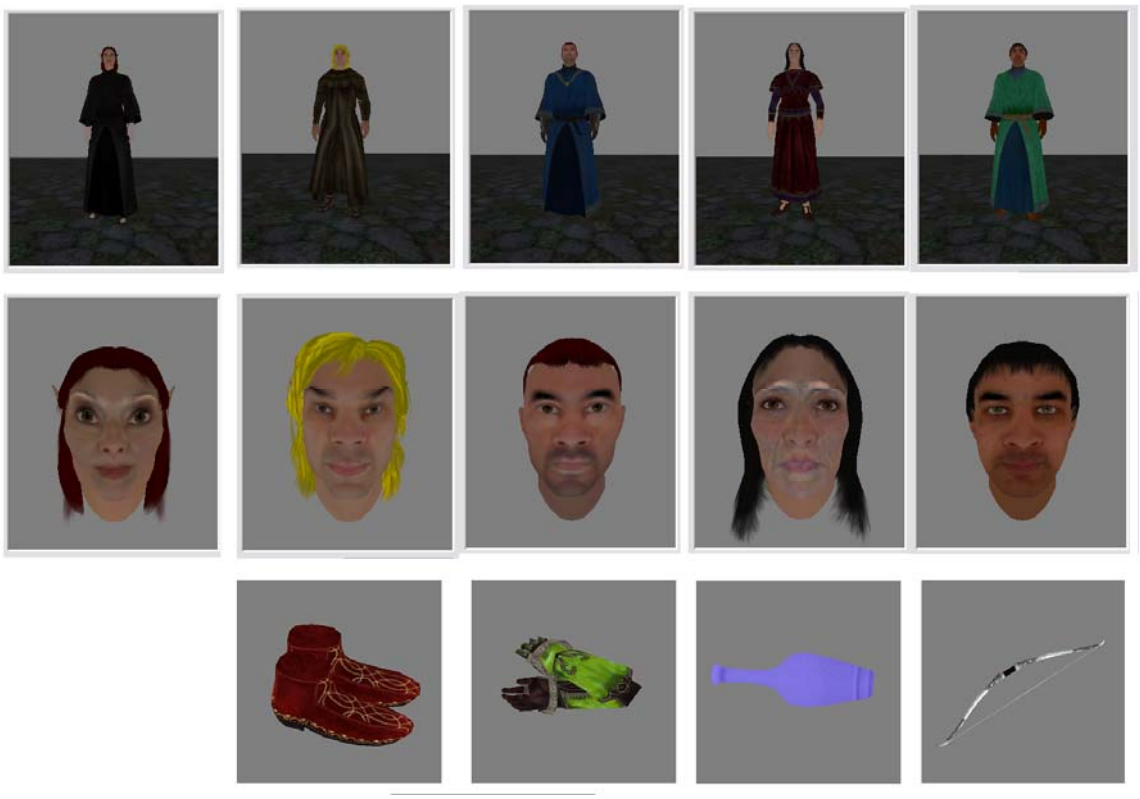
Appendix I

Objects and characters of the neutral VR task.
The left-most character was not involved in the recall task.



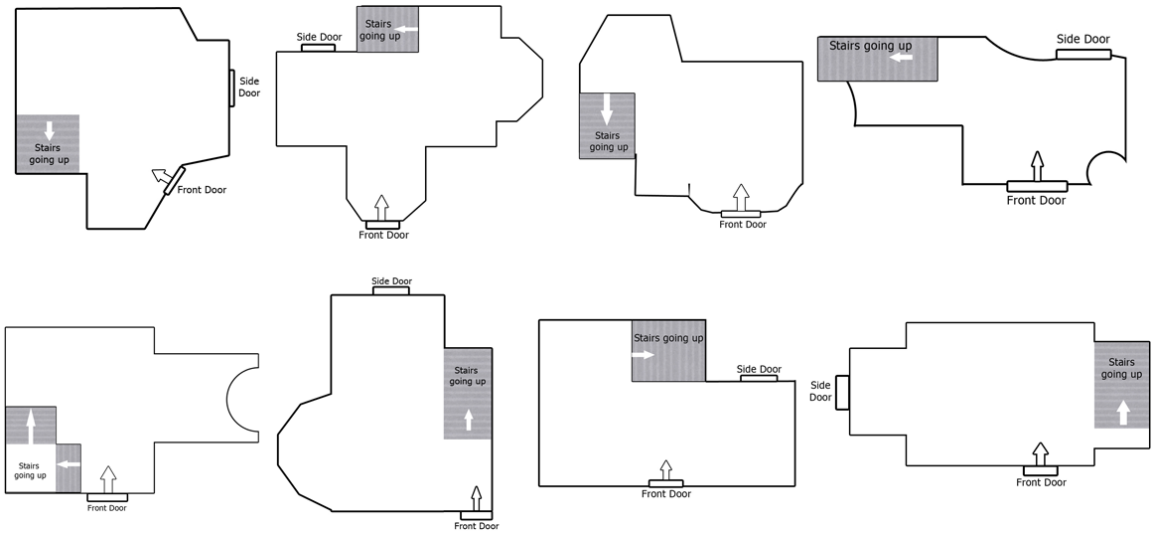
Appendix II

Objects and characters of the emotional VR task.
The left-most character was not involved in the recall task.



Appendix III

The spatial layout of locations in the VR task. Locations of the emotional task are presented in the upper row, and those of the neutral task are presented in the lower row.



Appendix VI
An example of a completed memory questionnaire.
The actual questionnaires were in PDF form

Dream and Nightmare Laboratory	Participant 21	Memory Questionnaire C12

Email Phil at p.stenstrom@umontreal.ca for any questions.

For each question (expect the first), you must try to answer & you must indicate if:
1) you **remember** (you know the answer, and can visualize the event relating to the question).
2) you **know** (you know the answer, but you cannot remember the experience and the context which relates to the question).
3) you do **not** know the answer. Try to answer the question anyway, even if you guess.

For example, if the question is "what did you eat for breakfast?", then possible answers are:
- I remember: I remember sitting at the kitchen table, pouring milk on the cereal and then eating it while listening to the news.
- I know: I know I had cereal, but I can't remember any details about how I ate it.
- I don't know: I cannot remember what I had for breakfast. My guess is toast.

Please take a moment and try to remember visiting Borbas (the store owner)

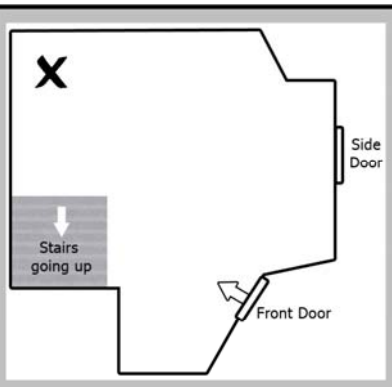
1.1 How well do you remember visiting Borbas? Well

1.2 Please write what Borbas told you

1.7 Please put an X indicating the location in which you talked to borbas.

Do you remember or know? I remember

1.8 What direction was Borbas facing when you talked to her? South



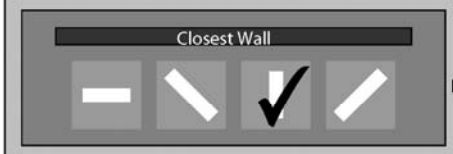
These questions concern Borbas

2.1 Age	Old	Do you remember or know?	I know
2.2 Accent	American	Do you remember or know?	I know
2.3 Hair Length	Long	Do you remember or know?	I remember
2.4 Hair Color	Black	Do you remember or know?	I remember
2.5 Clothing Color	Red	Do you remember or know?	I do not know
2.6 Clothing Type	Robe	Do you remember or know?	I do not know

The object on the table

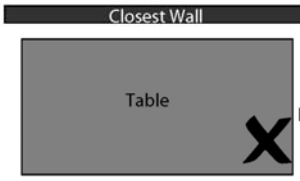
3.1 What was the object you had to retrieve?	Gloves	Do you remember or know?	I remember
3.1.1 What was the color the object?	Green	Do you remember or know?	I remember

3.2 What was the orientation of the object? (Click on the correct orientation below)



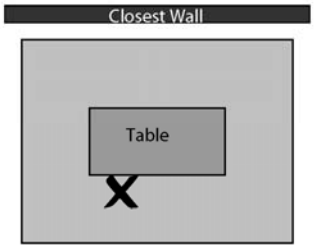
Do you remember or know? I know

3.3 Indicate the location of the **Object** on the table:



Do you remember or know? I know

3.4 Please indicate the location of the **Chair** that was around the table :

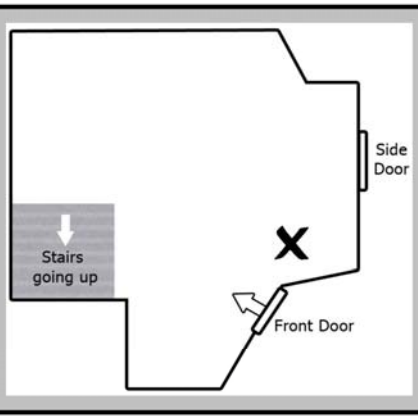


Do you remember or know? I know

LOCATION OF TABLE

3.5 Please put an X indicating the location of the table in the room.

Do you remember or know? I know



4.1 Please put an X indicating where the object on the **wall** was.

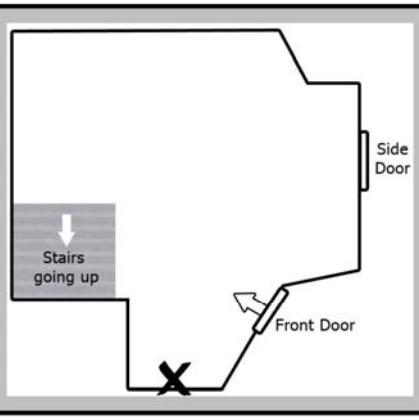
Do you remember or know? I know

4.2 What was on the wall? Painting

Do you remember or know? I remember

4.3 Can you give details about what was on the wall? Village

Do you remember or know? I know



4.4 Please put an X indicating where the furniture was.

Do you remember or know? I do not know

4.5 What furniture was in the room? Desk

Do you remember or know? I know

4.6 What object was on top of the furniture? Bowl

Do you remember or know? I remember

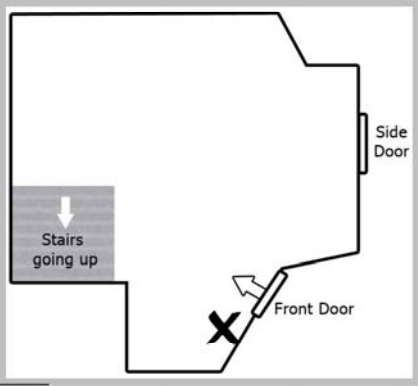
4.7 Where was this object on the furniture? Left

Do you remember or know? I know

4.8 What object was leaning on the side of the furniture? Broom

Do you remember or know? I remember

4.9 The object was leaning on which side of the furniture? Right



4.10 Please put an X indicating where the center of the **carpet** was.

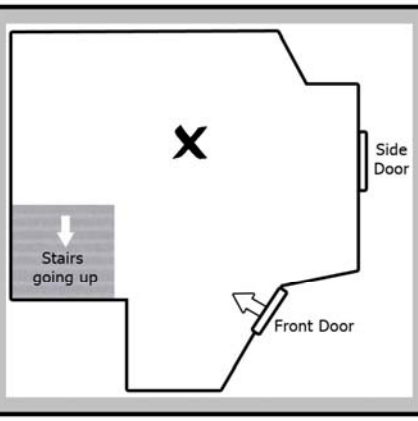
Do you remember or know? I know

4.11What color was the carpet? Green

Do you remember or know? I remember

4.12 What shape was the carpet? Round

Do you remember or know? I know

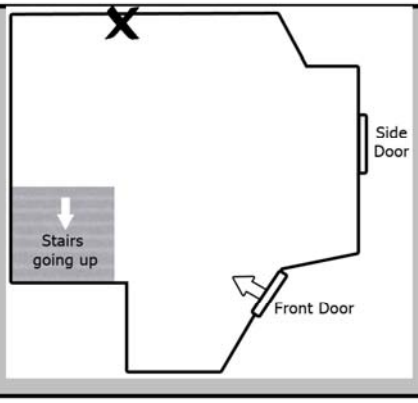


5.1 Please put an X indicating where the **fireplace** was.

Do you remember or know? I remember

5.2 What shape was the fireplace? Round Base

Do you remember or know? I know



6.1 In what building did you find Borbas? Write number here -->
Please write the number of the building indicated on the map below 19

Do you remember or know? I know

CHRONOLOGY

7.1 Who did you see **before** the Borbas? Aldos (the drunk)

Do you remember or know? I remember

7.2 Who did you see **after** Borbas ? Ulrich (captain of the guard)

Do you remember or know? I remember

End of questionnaire
Please save as a text file and email to p.stenstrom@umontreal.ca as soon as you are finished.
Thank you!